Eco-friendly sample preparation methods for enrichment of sulfonamide antibiotic residues followed by liquid chromatography analysis

Jedsada Jaroensan

A Thesis Submitted in Partial Fulfillment of Requirements for
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ABSTRACT

This work presents the preparation of two effective sorbents namely hydrophobic deep eutectic solvent impregnated on melamine sponge (HDES-MS) and Mg-Al layered double hydroxide combined with alginate beads (Mg-Al@Alg beads) as alternative sorbents for preconcentration of four sulfonamide antibiotics. Scanning electron microscopy (SEM), X-ray diffraction (XRD), Fourier Transform Infrared Spectroscopy (FT-IR) and N_2 adsorption were used to characterize the synthesis sorbents. The developed method was found to be advantageous as compared with other methods. In addition, the preparation of sorbents simple, short time and less consumption of toxic organic solvent. The greenness of the developed method was assessed using Analytical Eco-scale. The as-prepared sorbents were then extracted of sulfonamides and analysis by high performance liquid chromatography (HPLC) and ultra-high performance liquid chromatography (UPLC). The developed methods were applied for food and environment applications.

A fine tuning of hydrophobic properties of melamine sponges using hydrophobic deep eutectic solvent (HDES) was investigated as efficient sorbent for enrichment of sulfonamide residues in water samples. HDES were easily formed by tetrabutylammonium bromide (TBABr) and long-chain fatty acids and then dropped into the sponge before being utilized as sorbent in micro-solid phase extraction (micro-SPE) prior to HPLC analysis. The experimental parameters affecting the analytical performance were evaluated. The optimum conditions were 100 µL HDES2 (TBABr:dodecanoic acid), 0.7x0.7x0.7 cm^3 of MS size, 150 µL CTAB 0.03 molar and methanol 500 µL. Under the optimum conditions the linearity was in the range 10-3000 µg L^{-1}, the LODs were in the range 0.64 to 7.5 µg L^{-1} and LOQs were in the range from 1.92 to 22.5 µg L^{-1} and enrichment factor (EF) were in the range 4.00-5.33. Ultimately, the investigated extraction method was prosperously studied to the analysis of trace levels of sulfonamide residues in water samples.

Due to presence of free hydroxyl and carboxyl groups, alginates can be easily modified by different chemical modification methods. This work introduces a simple method for preparing uniform alginate-based materials with exceptional properties for micro-SPE method prior to UPLC-PDA analysis. LDH combined with alginate beads was synthesized and used as efficient sorbent. Various factors affected the extraction efficiency were evaluated. The optimum conditions were 1%w/v Mg-Al LDH (1:1 molar ratio), 0.5% alginate, 0.05 g of Mg-Al@Alg beads, CTAB (0.2 M, 150 µL) and 500 µL acetonitrile. The LODs were in the range 3-6 µg L^{-1}, the LOQs were in the range 9-18 µg L^{-1} and enrichment factor (EF) were in the range 19.53-43.40. The method has been applied to determine sulfonamide residues in honey samples.

Keyword : Deep eutectic solvent (DES) Layered double hydroxide (LDH) Liquid chromatography Sulfonamides Micro solid phase extraction (µ-SPE)

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Jedsada Jaroensan

TABLE OF CONTENTS

Page

LIST OF TABLES

Page

LIST OF FIGURES

Page

CHAPTER I

INTRODUCTION

1.1 Introduction

Antibiotics are an important class of pharmaceuticals which are frequently used in the treatment of bacterial diseases in humans and organism such as respiratory tract, digestive system, urinary system and skin infection. The use of antibiotics should appropriately consume to high benefit of patient and reduce problems after treat them such as overdose, drug use inappropriate for disease, drug resistance, antibiotic allergy and side effect from obtaining antibiotics [1]. Sulfonamide antibiotics (SAs) are known as extensively utilized antibiotics that widely used for treating disease from human and veterinary medicine and these antibiotics as one of the most important groups of pharmaceutically active compounds. They are also used to solve the problem and create a rising concern about new pollutants that excrete antibiotics from poultry animals towards the environment [2]. Amongst sulfathiazole (STZ) is group of sulfonamides family. It was detected in water resources for the sake of example drinking water [3]. sulfachloropyridazine (SCP) is one of the most commonly used because of its low cost broad-spectrum antimicrobial activity [4]. In recent years, SCP increasingly discharge in water including wastewater [5], river water [6], lake water [7], groundwater [8], and even tap water [9], has been expanded. To ensure consumer safety, the allowable level in food is usually defined by the maximum residue limit (MRL). The MRLs of sulfonamides restricted by the European Union [10], should not exceed 100 $\mu g\ kg^{-1}$. Due to the concern regarding the need to monitor trace levels of sulfonamides with high matrix interferences, sample treatment plays an important role in various applications.

High performance liquid chromatography (HPLC) [11,12] coupled with various detector, including UV, diode array detector (DAD), and mass spectrometry is a powerful analytical method for analysis of sulfonamide antibiotics. Although the mass spectrometry detector provides more sensitivity and selectivity than the UV for monitoring target compounds in complex samples, it is a very expensive and complex instrument [13]. Considering the presence of trace sulfonamide antibiotics in complicated real matrices, a suitable sample enrichment is needed [14] before their analysis. Although, HPLC is popular analytical technique. However, it can be an high cost method, it requires a large number of expensive organics, needs a power supply, and required regular maintenance [15]. Thus, ultra performance liquid chromatography (UPLC) is one of interesting analytical technique. Basically, it is an upgraded form of HPLC using high pressures, and offering distinguished peak resolution and sensitivity [15]. Moreover, this technique is great savings in time and solvent consumption wherewith, reducing cost of analysis [16]. Solid-phase extraction (SPE) a well-founded technique and has been used for sample preparation [17]. Although efficient, those SPE-based methods usually need long extraction times, a large of amount sample and reagent and labour-intensive [18]. Due to the rising concern regarding for the development of greener extraction techniques, micro-SPE has been investigated. Similarly, the analytes from the surface of the small amount of adsorbent are eluted by a suitable elution solvent. Reversed phase sorbents are inappropriate for more polar or ionized molecules such as sulfonamides [19]. Different sorbents have been used including Hydrophilic-Lipophilic Balanced (HLB) column [20], activated carbon [21], biological sorbents [22], covalent organic frameworks (COFs) [23], carbon nanotubes [24] and graphene [25] etc. Therefore, investigating a specific sorbent which have a large and highly specific surface area to provide large number of hydrophilic interaction sites to polar compounds [26].

Currently, porous materials have become progressively pleasing due to the excellent separation efficiency. Polymer sponges such as melamine sponges (MS) have attracted significant concentration caused their low density, high porosity and three-dimensional (3D) skeleton structures [27]. In order the modified the property of melamine sponges from hydrophilicity [28] to exhibit a superhydrophobic behavior, therefore the surface of the melamine sponges has to be modified [29]. Consequently, the adsorptive property and selectivity of the sponge increase, provide a large variety of pragmatic applications [30].

Nowadays, attention be paid in green analytical chemistry [31]. Moreover, green solvents have been used in many applications, such as catalysts, mobile phase additives [32], modification of sorbents/materials [33] and extraction solvents [34]. Several environment-friendly solvents such as surfactant, ionic liquid, deep eutectic solvent, have been used. Currently, deep eutectic solvents (DESs) are attracting great interest as alternatives to conventional organic solvents and ionic liquids (ILs) [35]. DESs can be easily assembled by hydrogen bond interactions of a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) compounds [34,35] at invested temperatures with regular agitation. They could be separated as hydrophilic DESs and hydrophobic DESs in agreement with their polarity [36,37]. More recently, hydrophobic deep eutectic solvents (HDES) have received much attention than hydrophilic DES, due to enlarging the probable applications and increasing efficiencies [40], in addition to being sustainable, and low cost. The HDES are easily to generate by low solubility in water compounds, with long-chain fatty acids (such as octanoic, decanoic, or dodecanoic acids) as HBDs, and menthol (a natural monoterpene-having very low solubility in water) as HBAs [41]. However, a few literatures describe studies on the sponges impregnated by DES for the removal of pesticides and dyes from water [38] and removing oil from water [29].

Layered double hydroxides materials (LDHs) are a class of synthetic 2D nano-structured inorganic materials that have positively charged layers of metal hydroxides, between which are located anions and water molecules [42]. The extraordinary properties of LDHs like tunability, exchange interlayer anion abilities, large surface area, thermal stability and easily preparation [43]. These great features, LDHs have been used in variety fields for example, electrochemistry [45,46], adsorption [47,48], catalysis [48] and biotechnology and medication [50,51]. Although LDH is widely used for various purposes, the application of LDHs for extraction is few reported for removing anionic compounds. Because the anionic compounds are laborious to be eluted by the commonly used organic solvent toward the strong ionic interaction between anions and LDHs [43]. Moreover, resulting the material is in the form of powder and particles, led to separation and regeneration of them, are time-consuming and energy-consuming which limits its application in practical applications [51]. Therefore, the development of alternative adsorbents by using LDH materials for improvement of the extraction for target analytes are interesting and challenging. However, it should be noted that the improvement of adsorption performance was achieved through surface modification of LDHs by organic compounds [53–55].

However, modifications with organic compounds made much more challenging in terms of subsequent handling or disposal, wherewith the environmental concerns [55]. Therefore, it is important to develop sorbents with good performance that are environmentally friendly.

To solve these problems, the use of bio-based materials either as main materials or intercalated with other materials is a great choice for sustainable and green chemistry [55]. Sodium alginate is a naturally occurring anionic linear polysaccharide made up of alternating blocks of α-L-guluronic and β-D-mannuronic acid residues that are linked by 1–4 bonds through intermolecular cross-linking to form hydrogels, films, and microbeads with cations such as Ca^{2+} [52,57]. That exists in naturals such as brown algae, the Sargassum's cell wall, and also specific bacteria [57]. These neutral anionic polymers, sodium alginate, have the benefit of being abundant, inexpensive, non-toxic, biodegradable and various their functional groups [59,60]. Therefore, sodium alginate is an interesting choice to use for combined with LDHs for the alternative sorbent improvement to extract target analytes from real samples.

In the present work, an eco-friendly melamine sponges impregnated by hydrophobic deep eutectic solvents and layered double hydroxide (LDHs) combined with alginate beads (LDHs@Alg beads) were synthesized for the extraction of sulfonamide residues prior to chromatography analysis. Selected optimum of two alternative sorbents were prepared, and theirs physicochemical and structural properties were analyzed. The HDESs were then impregnated on the pore of the melamine sponges (HDES-MS), while the beads composed of layered double hydroxide and alginate was synthesis using as sorbent in micro-solid phase extraction (micro-SPE). The morphology and structure of this obtained composites were systematically studied by a series of characterizations. The extraction factors were investigated by a univariate experimental design. The proposed methods were then applied for the analysis of sulfonamides in environmental real samples. The greenness of the proposed approach was assessed by the Analytical Eco-scale and Analytical GREEnness metric (AGREE) approaches.

1.2 Objectives

1.2.1) To develop melamine sponge impregnated hydrophobic deep eutectic solvent and layered double hydroxide combined with alginate beads as alternative adsorbent for micro solid phase extraction method for preconcentration of four sulfonamide antibiotics including sulfatiazole (STZ), sulfacloropyridizine (SCP), sulfamethoxazole (SMX) and sulfadimethoxine (SDM)

1.2.2) To apply the established approach to determine low level SAs concentration in real samples

1.3 Scope of research

1.3.1) The method will be validated by the following parameters: calibration curves, limits of detection (LOD), limits of quantitation (LOQ), and reproducibility.

1.3.2) The preconcentration method will be studied for determination of some SAs residues in water and honey samples.

1.3.3) Developed method will be applied to analysis of SAs residues in water and honey samples.

1.4 Benefit of research

1.4.1) The optimized conditions for preconcentration method of some SAs using melamine sponges impregnated hydrophobic deep eutectic solvents and layered double hydroxide combined with alginate beads as sorbent in extraction method.

1.4.2) Trace SAs residues contents in food samples will be obtained.

1.5 Definition of terms

1.5.1) The preconcentration procedure aims to increase the concentration of a sample prior to analysis or detection.

1.5.2) The limit of detection (LOD) is the lowest quantity of analyte that can be domineered to absence of analyte within a stated confidence limit.

1.5.3) The retention time is the run time between the time of injection of a solute and the time of elution of the peak maximum of that solute.

1.5.4) Resolution is the good signal of some SAs residues and the peaks were obtained.

1.5.5) Extraction efficiency is the good percentage recovery of micro solid phase extraction obtained.

CHAPTER II
LITERATURES REVIEW

2.1 Sulfonamide antibiotics (SAs)

Sulfonamides (SAs) are synthetic bacteriostatic antibiotics that competitively inhibit conversion of p-aminobenzoic acid to dihydropteroate, which bacteria need for folate synthesis and ultimately purine and DNA synthesis. Most sulfonamides are easily absorbed orally and, when applied to burns, topically. After adsorption, sulfonamides are distributed throughout the body. They are metabolized mainly by the liver and defecated by the kidneys [60]. Sulfonamide was firstly noted as anti-bacterial in 19th century by Gerhard Domagk who is a Nobel Prize winner in 1939. In his attempt to save daughter from streptococci killing infection, he observed that prontosil; a sulfonamide dye, is able to selectively prohibit the infectious bacteria cells. In 1936, Ernest Fourneau discovered that this dye was a pro-drug. It, actually changes in human body to sulfanilamide which is the anti-bacterial active agent [61]. SAs structures are organo-sulphur compounds containing and a variant five to six membered heterocyclic rings. SAs are not arduous biodegradable and have potential to cause various unfavorable side effects including diseases of the digestive and respiratory tracts. The typical structure of SAs including a sulfur atom as center atom, with two double bonded with two oxygen atoms, that is also bonded to a nitrogen atom (existing as a substituted amine) and an aniline group (the -SO_2NH_2 and/or -SO_2NH- group) and are characteristic of the existence of sulfanilamide group. Sulfonamide with multitudinous substituent groups exhibits different biological activities, particularly nitrogen and oxygen donor ligands. Sulfonamide functional groups are good antimicrobial agents, mainly when influenced by the substituent groups is present in the aromatic rings [43,44]. Over the years, these compounds have been used to treat and cure a variety of ailments in living beings for example antibacterial, antiviral, anti-inflammatory, diuretic [64]. In addition to the ability of this group of compounds to inhibit a wide range of diseases, in recent years their ability to inhibit carcinogenicity has also been reported [65]. Although SAs have various advantages and are widely used or in excessive amounts in animal husbandry, there is a possibility that these substances may remain in organism and environment [66]. If there is a sufficient amount of residue of this group of substances, it may cause side effects from using this group of substances, such as: hypersensitivity reactions, crystalluria, hematologic reactions [60]. Recently, there have been reported of residue levels of these compounds in environmental samples and in various organisms, such as sulfamethoxazole (SMX) is the most frequently detected antibiotic in wastewater treatment plants reaching levels up to 77,400 ng L^{-1} in influent and up to 68,700 ng L^{-1} in effluent wastewater [67], for sulfadiazine was detected in swine manure [68]. Therefore, it is necessary to limit the amount of residue of SAs be within the specified amount for safety, the allowable level in food is usually defined by the maximum residue limit (MRL). The MRLs of sulfonamides restricted by the European Union [10] should not exceed 100 µg kg^{-1}. The structures of the four sulfonamides studied in this work are shown in Table 1.

Table 1 Structures of SAs used in this work.

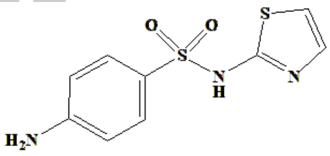
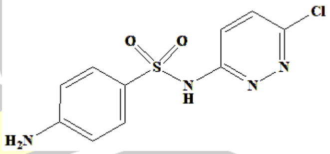
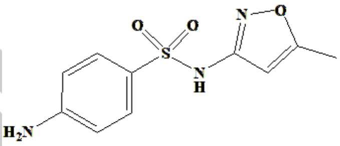
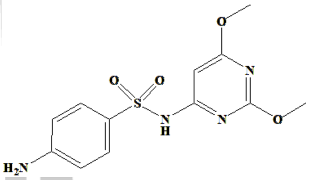
Name	pKa	log Kow	Formula	Structure
Sulfathiazole (STZ)	7.27	0.53	$C_9H_9N_3O_2S_2$	
Sulfachloropyridazine (SCP)	6.6	0.85	$C_{10}H_9ClN_4O_2S$	

Table 1 Structures of SAs used in this work (continued).

Name	pKa	LogKow	Formula	Structure
Sulfamethoxazole (SMX)	6.16	0.89	$C_{10}H_{11}N_3O_3S$	
Sulfadimethoxine (SDM)	6.91	1.08	$C_{12}H_{14}N_4O_4S$	

2.2 Application of hydrophobic DES for sulfonamide preconcentration

The selection of solvent is the one thig necessary decision to be taken when designing an extraction procedure, as extraction solvents play a key role in determining the analytes quality, quantity, and selectivity. The principle of consideration in selecting the extraction solvent should take solubility of the analytes with the extraction solvent, also known as “like dissolve like”. Extraction solvents commonly used consist of polar solvents such as water, methanol and non-polar solvents for instance hexane, chloroform. These extraction solvents have high potential for extracted analytes. In the other side, organic solvents have a number of disadvantages such as most of them are volatile and toxic and contribute significantly to environmental pollution [69]. To solve toxicities, with the development of green chemistry, recently, present alternative solvents among proposed green solvents, ionic liquids, natural deep eutectic solvents, supercritical and subcritical fluids and solvents from natural and renewable sources stand out as the most promising approaches for current solvent improvement [70].

One of alternative solvent in term of salts is present in liquid state at room temperature. Such salts, called “ionic liquids (ILs)” form a relatively new class of solvents, which have, by convention, a melting point below 100°C (at 1 atm). It was discovered 19th century, when Paul Walden reported that ethylammonium nitrate

$(C2H_5NH_3^+\ NO_3)$ melts at 12°C. Research more interested during the 1990s, with exponential multidisciplinary publication rise on the topic, lastly becoming a major subject of study for modern chemistry and a distinctive research field, with sumptuously publications each year [71]. even though, ILs are quite interesting however, due to ILs elevated cost [72] the environmental effects of such exceedingly stable compounds are now widely considered, as ILs can be toxic at environmental and nutrition levels [73].

Deep eutectic solvents (DESs) containing a mixture of organic compounds (a hydrogen-bond acceptor (HBA) and a hydrogen-bond donor (HBD)). Several DESs can be simply prepared from a binary mixture of an uncharged HBD (amide, amino acid, sugar, alcohol, amine, or carboxylic acid), and a HBA, such as a quaternary ammonium salt [55,56]. DESs has similar properties ILs for example: non-flammability, high chemical and thermal stability. Furthermore, as ILs, DESs are highly tunable, by altering components compositions and their molar ratios. Their main advantages over ILs are lower cost of the raw materials, easier preparation, lower toxicity and higher biodegradability [76]. Therefore, in over years, DESs represent a nascent class of sustainable solvents with ever-increasing applications[74].

Liu et al. (2017) [77] investigated a simple, inexpensive and sensitive method named emulsification liquid–liquid microextraction based on deep eutectic solvents (ELLME-DES) for the extraction of sulfonamides (SAs) from water samples followed by HPLC-UV, including sulfadiazine (SDZ), sulfamerazine (SMR), sulfametoxydiazine (SDD) and sulfamethoxazole (SMX). It showed highly satisfactory results and potential for rapid extraction of SAs from water samples combining with the method of ELLME-DES. Under optimum conditions were when the parameters were 193 mL of DES4 (ChCl:Phenol), 100 mL of THF and an ultrasonication time of 17 min. The recoveries of four SAs were in the range 74.65 to 88.48%. This procedure was successfully applied to the determination of target analytes in spiked water samples.

Pochivalov et al. (2021) [78] suggested a novel approach for liquid-liquid microextraction via formation of hydrophobic deep eutectic solvent by pH adjusting for sulfamethazine, sulfamethoxazole, sulfaquinoxaline and sulfadiazine in milk samples. The proposed approach enables one to avoid heating and usage of auxiliary energy sources, which considerably simplifies the procedure and minimizes the extraction time in comparison with the existing analogues. The nature of precursors played an important role in the extraction process, providing different types of interaction with the analytes. The preconcentration factors rising with an increase of hydrophobicity of the analyte. In situ formation of fine droplets of the solvent provided fast mass-transfer of sulfonamides. The limits of detection of four SAs were equal to 1-5 µg L^{-1}.

Díaz-Álvarez et al. (2022) [79] proposed the use of a hydrophobic natural deep eutectic solvent (NADES) as supported liquid membrane (SLM) for hollow fiber liquid-phase microextraction (HF-LPME) of sulfonamides from water. The combination of formic acid:L-menthol (1:1) was selected as optimum since it provided a better and more balanced extraction of SAs. The developed method was applied to SAs extracted in artificial water containing humic acids, tap and river water samples, The result provided a good clean-up ability for all the tested samples, there are good linearity for all the SAs and samples with r^2 greater than 0.992. Relative recoveries ranged from 53 to 121%, with relative standard deviation values between 5 and 21%, the low limits of detection of the method.

García-Valcarcel et al. (2024) [80] evaluated natural deep eutectic solvents (NADES) as sustainable solvents in the development of an ultrasound (US)-assisted extraction method for sulfonamides from soil samples. Under optimum conditions the ChCl:1,3-propanediol in a molar ratio of 1:4 was used for SAs extraction under US assisted, recovery was in the acceptable range with relative standard deviations (RSDs) lower than 8 % were obtained. In addition, the proposed method is shown good SAs preconcentration potential in real samples.

Arshia Alizadeh Irani et al. (2024) [81] developed sample pretreatment method based on the combination of counter current salting-out homogenous liquid–liquid extraction and magnetic deep eutectic solvent-based dispersive liquid–liquid microextraction for the extraction of some sulfonamide antibiotics from chicken meat samples. For this purpose, the extracted analytes was taken and injected into DI water after mixing with magnetic deep eutectic solvent is Choline: 4-chlorophenol$]^{+}[FeCl_4]^{-}$. Then, the magnetic deep eutectic solvent droplets were separated in the presence of an external magnetic field followed by quantitative analysis. This work provides interesting step for phase separation by magnetic assisted resulting in the easier extraction process. The developed method also indicates the low limits of detection and quantification, high extraction recovery and good precision were obtainable by using the offered method.

2.3 Application of modified melamine sponge as adsorbent

Sample preparation represent elementary steps of an analytical procedure is even more critical whether or not the sample matrices are uncomplicate or complex to ensure that the analytes are satisfactorily isolated, cleaned up, and enhanced in the final extract, and are in a state that is compatible with the interested analytical technique [82]. Essentially, the procedure originated by Tswett as known as solid-phase extraction (SPE) which was commercially introduced in the late 19th century. Nowadays, SPE remains one of the most widely-used sample preparation procedures for treating liquid matrices. Over the past 15-20 years, there have been extensive studies involving the miniaturization of SPE with retention of the traditional constructs. Due to SPE technique has some limitations for instance: difficult, time consuming, require many purification steps and the special adsorbents involved are costly [65–67]. The micro-SPE (μ-SPE) has been used in many such SPE studies in reference to the trend toward miniaturization, with the “μ” designation mean to signify reduction in device equipment, reduced amount of sorbents especially, the materials with their advantageously large surface area and excellent physicochemical properties [86]. Therefore, in this work, there is interest in using melamine sponges as absorbents toward environmentally friendly, 3-dimensional framework, low cost, low density, multi-porous, modifiable to functionalization in order to tune its hydrophilicity or render it hydrophobic and easy modification. Moreover, the open pore structure of the sponge enables it to trap and immobilize adsorbent particles within its network of interconnected pores [68,69]. Recently, melamine sponge was modified with various processes was reported for used as adsorbents for adsorbed different kind of analytes.

Lei et al. (2017) [89] inspired by the development of smart oil/water separation materials, when contacting with different pH water droplets in air, the as-prepared product shows excellent switchable wettability between super hydrophilicity (0°) and highly hydrophobicity (135°). pH responsive melamine sponge has been obtained by grafting poly (4-vinylpyridine) on the skeleton surface through atom transfer radical polymerization. Meanwhile, this responsive sponge also exhibits super-hydrophilic/oleophobic property and highly hydrophobic/super-oleophilic property in pH 1 and 7 respectively. The modified melamine also quickly releases the absorbed oil underwater without leaving any residues and hurting the environment nearly, showing a good potential in controlled oil/water separation and oil recovery.

Makoś-Chełstowska et al. (2023)[29] evaluated the extensive extraction of oil from the bottom of seas and oceans and its transportation. In this paper presents the preparation of a simple impregnation of a melamine sponge with deep eutectic solvents (DES), which can be obtained from natural sources and the preparation of DES-MS is simple and involves little time and consumption of toxic organic solvents. The result provided the highest absorption capacities were obtained for MS impregnated with tetraethylammonium chloride and decanoic acid in a 1:2 M ratio as superhydrophobicity, superoleophobicity, low density, high porosity, high thermal, mechanical, and chemical stability, and the possibility of multiple regenerations without loss of sorption capacity. This work indicate that DES-MS may be a “green” and low-cost alternative to current approaches for removing oil from water.

Zeng et al. (2023) [90] in this study, a chitosan–melamine sponge (CTS–MS) composite as a promising adsorbent material with excellent regeneration, easy separation and high adsorption capacity. The obtained CTS–MS composite was employed to evaluate the adsorption properties towards Orange II (OII) anionic dye in wastewater. The entire adsorption process was found to be spontaneous and endothermic in nature. More importantly, the new composite could be directly separated and desorbed effectively, this sorbent can be reused in 10 cycles. Under optimal conditions, the fast adsorption equilibrium.

2.4 Application of chromatography techniques for sulfonamide detection

Table 2 Sulfonamide antibiotics detection with chromatography techniques.

Author	Technique	Chromatographic condition
Kim et al. (2016) [91]	HPLC-PDA	**Column:** Unison UK-C18 (150 mm×3.0 mm, 3 µm particle size) (Tokyo, Japan) 126 column at 30 °**C** **Mobile phase:** A (0.1% acetic acid in PBS) and B (0.1% acetic acid in methanol) **Injection volume:** 3 µL **Flow rate:** 0 0.4 ml min^{-1} **Wavelength:** 270 nm
Dowlatshah et al. (2021) [92]	HPLC-DAD	**Column:** LiChroCART 75-4 Purosphere STAR RP-18e 3mm (75 mm x 4.0 mm i.d.) (VWR, Germany) proceeded by a guard column Kromasil1 100 A, ˚ C18, 5mm (20 mm x 4.6 mm i.d.) (Scharlab S.L., Barcelona, Spain). **Mobile phase:** 0.1 % formic acid (pH 2.6) (component A) and acetonitrile (component B). **Flow rate:** 0.8 mL min^{-1}. A gradient program was used from 85 % A to 70 % A in 10 minutes for the separation. **The injection volume:** 7 µL. **The wavelength:** 254 nm.
Patyra et al. (2019) [93]	HPLC-FLD	**Column:** Zorbax Eclipse XDB C18 chromatographic **Mobile phase:** 0.08% acetic acid in Milli-Q water, methanol, and acetonitrile with a gradient elution. **Run time:** 25 min

Table 2 Sulfonamide antibiotics detection with chromatography techniques (continued).

Author	Technique	Chromatographic condition
Shahriman Et al. (2021) [4]	HPLC-DAD	**Column:** Ascentis®C18, 5 µm particles size (150 mm × 4.6 mm) separation column (Supelco®, Bellefonte, PA, USA) by gradient elution **Mobile phase:** (A) 1% acetic acid in an aqueous solution and (B) acetonitrile (75:25, v/v) **Flow rate:** 1.0 ml min^{-1} **Injection volume:** 10 µL. **Wavelength:** 269 nm
Ma et al. (2023) [94]	UPLC-PDA	**Column:** XBridge Shield RP C18 column (4.6 x 250 mm, 5 µm) **Mobile phase:** A was 0.1% (v / v) formic acid and mobile phase B was methanol. **Flow rate:** 0.7 mL min^{-1} **Injection volume:** 25 µL **Wavelength:** 273 nm
Sun et al. (2023) [95]	UPLC-PDA	**Column:** BEH C18 column (50 mm x 2.1 mm, 1.7µm) **Mobile phase:** 0.1%formic acid aqueous (A) /acetonitrile (B) with gradient mode **Flow rate:** 0.2 mL min $^{-1}$ **Injection volume:** 10 µL. **Wavelength:** 270 nm

Table 2 Sulfonamide antibiotics detection with chromatography techniques (continued).

Author	Technique	Chromatographic condition
Ma et al. (2024) [96]	UPLC-MS	**Column:** Agilent ZORBAX XDB-C18 column **Injection volume:** 3 mL **Flow rate:** 0.3 mL min^{-1} **Mobile phase:** 0.1% formic acid solution (mobile phase A) and acetonitrile (mobile phase B) with gradient mode **MS mode:** positive mode, the electrospray ionization (ESI) source was used for ionization analysis and the MRM mode
Huang et al. (2024) [97]	UPLC-MS	**Column:** C18 column (100 mm × 2.1 mm, 1.7 µm) by gradient elution at 35 ˚C. **Mobile phase:** Water+0.1% Formic acid (A) and acetonitrile +0.1% Formic acid (B) with gradient mode **Flow rate:** 0.25 mL min^{-1}. **Injection volume:** 1.0 µL

2.5 Layered double hydroxide (LDHs)

Layered double hydroxides are one of the variety of names given to a family of layered materials first discovered in Sweden in 18th century. Layered Double Hydroxides (LDHs) are 2D ionic lamellar materials as anionic clays categories. The structure of LDHs is based on brucite-like layers containing both divalent Metal II and trivalent Metal II cations coordinated to six OH^- hydroxyl groups [98]. It can be expressed by the formula $[[M^{2+}_{1-x} M^{3+}_{x} (OH)_2]^{x+} (A^{n-})_{x/n}] mH_2O$. Where metal II and metal III are divalent cation such as Mg^{2+}, Ni^{2+}, Ca^{2+}, Cu^{2+}, Mn^{2+}, Co^{2+} or Zn^{2+} and trivalent cation such as Al^{3+}, Cr^{3+}, Ga^{3+} or Fe^{3+}, respectively. The value of x is equal to the molar ratio of $M^{3+}/ (M^{2+} + M^{3+})$, whereas A is the interlayer anion of valence.

The identities of M^{2+}, M^{3+}, x, and A^{n-} may vary over a wide range, thus giving rise to a large class of isostructural materials with varied physicochemical properties [99].

The structure of an ideal LDH is based on $M(OH)_6$ edge-sharing octahedral units forming lamellas which are stacked on top of one another to form a 3D structures (as shown in Figure 1). LDH sheets achieve a net positive charge owing the substitution of a certain fraction x of the divalent cations with the trivalent ones. These positive charges are balanced by a variety of possible and anions exchangeability intercalated between the lamellas together with H_2O molecules [98]. The interlayer of LDHs consist of anions, water molecules and, in some cases, other neutral or charged organic/inorganic species [100]. The important characteristics of LDHs is that these moieties are generally weakly bound to the host lamellas. can be grouped as halides, Non-metal oxoanions, oxometallate anions, anionic complexes of transition metals, organic anions, anionic biomolecules and anionic polymers.

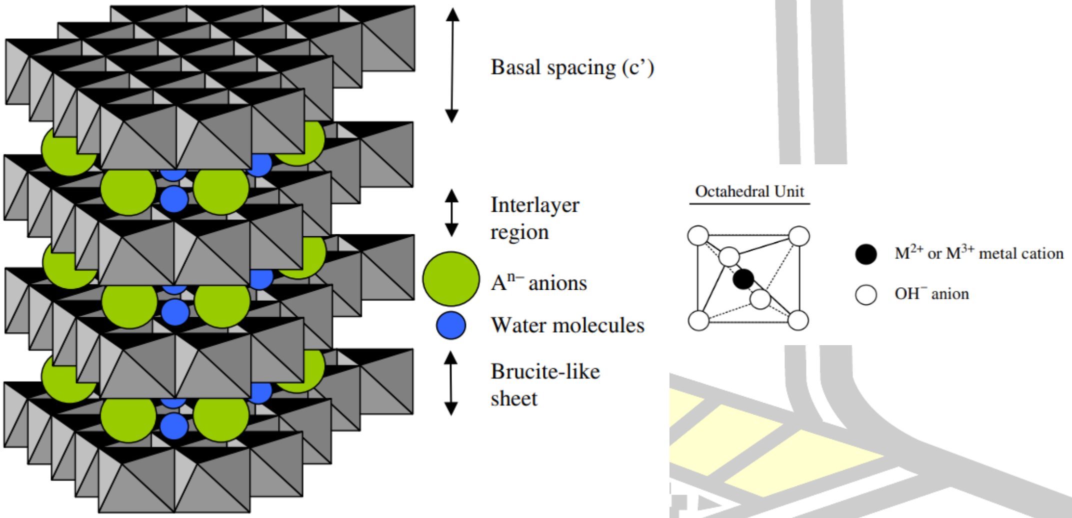


Figure 1 Scheme of LDH structure by Goh et al. [99]

Normally, the simplest and most commonly used method is coprecipitation. In this method, aqueous solutions of M^{2+} and M^{3+} concluding the anion that is to be incorporated into the LDHs are used as precursors. In order to ensure simultaneous precipitation of cations, it is essentials to carry out the synthesis under conditions of supersaturation. Generally, there are two kinds of coprecipitation conditions are coprecipitation at low supersaturation. Coprecipitation at low supersaturation is performed by slow addition of mixed solutions of divalent and trivalent metal salts at the selected ratio into a reactor containing an aqueous solution of the desired interlayer anion. Then, solution of an alkali is then added into the reactor simultaneously at such a rate as to maintain the desired pH for coprecipitation of the two metallic salts. For coprecipitation at high supersaturation requires the addition of a mixed salt solution to an alkaline solution containing the desired interlayer anion. However, coprecipitation at high supersaturation gives rise to less crystalline materials compared to those with low supersaturation, owing the formation of a large number of crystallization nuclei. After precipitation at low and high supersaturation, a thermal treatment process is performed to increase the yields and crystallinity of the materials follow by aging process [100,101]. The prepared LDHs are of great interest for nano materials science and technology (NMST), it can be used in various fields due to their special structural and unique applications for instance catalysis [103], pharmaceuticals [104], polymer additives [105], modified electrodes [105,106] and adsorbents [107,108] etc. With their layer positive charge, anion in interlayer, large surface area, thermal stability and resistant structure to water. Since, LDHs adsorbents are potentially good for a various anions, they are proposed as potential substitutes for commercial and dangerous expensive sorbents [42]. Conversely, numerous micro/nanoscale powdered adsorbents face the problems of poor reusability and difficult separation, which severely restrict their application in effluent treatment [91,109]. To solve the problems, in recent years, this nanomaterial has been combined with other materials to increase their adsorption efficiency, environmentally friendly and easy to use. The bio-based materials is the one of interesting material to combined with LDH materials because of a great choice for sustainable and green chemistry [55]. So, the combination of LDHs and bio-based materials as anion adsorbent are interest. In a few years ago the LHDs combined with the bio-based materials as adsorbent were reported. It can be seen that most of LDH combined with bio-based as adsorbent is on heavy metals, anions, organic and some inorganic, but there are very few reports on the use of LDH-based as an adsorbent for sulfonamide adsorption [111]. Therefore, it is a challenge to develop adsorbent-based LDH combined bio-based materials for the preconcentration of sulfonamide from real samples.

Li et al. (2018) [112] presented the preparation of nanocomposite beads prepared from Mg-Al-CO_3 LDH nanoparticles and chitosan for Se (IV) removal. The synthesis of the nanocomposite beads is achieved by direct mixing or in-situ synthesis of the LDH nanoparticles into the chitosan matrix. The results indicate that the in-situ synthesis of LDH inside the beads leads to several favorable characteristics, such as a higher mass loading of LDH and better dispersion of the nanoparticles, while displaying good selenium removal over a wide pH range, superior sorption capacity. The maximum adsorption capacities which is higher than reported capacities obtained in chitosan beads embedded with other nanocrystalline metal oxide fillers. These results show that the LDH/chitosan nanocomposite beads are promising alternatives to granulated media for selenium removal and sheds light on how best to design and fabricate high performance and sustainable nano-enabled sorbents.

Wang et al. (2018) [113] synthesized alginate-NiFe-LDH-S hydrogel (NFLS-gel) and applied as a new monolithic column for the selective enrichment and determination of heavy metal ions in food samples with simplicity, time-saving, selective and cost-effective environmentally friendly synthesis method improved adsorption capacity and effective elution. This new type of monolithic column with the incorporation of sulfide intercalated LDHs nanosheets provides more adsorption sites and enables the high selectivity of Pb(II) from mixtures containing a large excess of other interfering ions. Moreover, the as prepared monolithic column was successfully applied for the extraction of Pb^{2+} in water and drinking samples.

Lucas et al. (2019) [114] synthesized MgAl-LDH-biochar composites using co-precipitation method, there was a change in the structure of the adsorbent and increased randomness during the fixing of the dye. The composites were applied to remove an organic dye from aqueous solutions by physical nature adsorption in pH 12, with a removal > 95% for all composites. It was obtained a high adsorption capacity.

Lai et al. (2020) [115] demonstrated a phosphate-selective sustainable method by adopting Garcinia subelliptica leaves as a natural bio-template, where MgMn-layered double hydroxide (MgMn-LDH) and graphene oxide (GO) can be grown in situ to obtain L-GO/MgMn-LDH. Besides, Garcinia subelliptica leaves contain biflavonoids and triterpenoids, which can intercalate into LDH layers and facilitate ion access to the LDH composite, leading to high phosphate adsorption capacity. After calcination, the composite shows a hierarchical porous structure and selective recognition of phosphate, which achieves significantly high and recyclable selective phosphate adsorption capacity and desorption rate. These results indicate the proposed bio-templated adsorbent is practical and eco-friendly for phosphorus sustainability in commercial wastewater treatment.

Mohiuddin et al. (2021) [55] synthesized starch-Mg/Al layered double hydroxide (S-Mg/Al LDH) composites by eco-friendly co-precipitation method to quantification of six non-steroidal anti-inflammatory drugs (NSAIDs) was conducted using real samples by GC-MS. The proposed method was proven to be efficient and fast solid phase extraction (SPE) sorbents for NSAIDs. The developed method exhibited advantages over traditional solid phase sorbents such as good resolution, sensitivity, reproducibility, and specificity even in complex matrices with low limits of detection due to their high porosity and layered structure. addition, each LDH-SPE cartridge showed good reusability up to 30 cycles without a noticeable change in performance.

Karthikeyan et al. (2021) [116] showed the preparation of LDHs functionalized beads of the biopolymeric background using fabricated by a one-pot process ZnFe-LDHs composite and sodium alginate were used as the starting material. ZnFe-LDHs assembled alginate (ZnFe-LDHs@Alg) beads to adsorptive removal of the phosphate and nitrate anions from watergoverned by surface complexation, ion exchange and electrostatic force of attractions had demonstrated as the possible mechanisms. The developed method indicated great removal efficiency and percentage were examined along with various influencing factors. ZnFe-LDHs@Alg beads can be used as an efficient and selective sorbent for the remediation of toxic ions from water/wastewater samples.

Long et al. (2022) [57] synthesized a new type of adsorption material for Ni/Fe-LDH coated with sodium alginate (SA) by a simple hydrothermal method and treated with NaOH for Ni^{2+} and Cu^{2+} adsorption from water samples. The experimental results show that the prepared Ni/Fe LDH-SA adsorbent has high adsorption capacity at 25 °C. It has good performance when pH ≥ 7, and after four cycles, the removal rate of the two ions remains above 80% indicating good stability. The analysis mechanism shows that the removal process is mainly through physical adsorption precipitation, electrostatic adsorption, ion exchange, and chelation. Compared with traditional adsorbents, the adsorbent prepared in this study is easy to be recycled and reused, and has potential application value to other heavy metal ions. It is a promising adsorbent material.

CHAPTER III
EXPERIMENTAL

3.1 Chemicals and Reagents

All chemicals and reagents were analytical grade or higher. They were obtained from various suppliers, as shown in Table 3. Melamine sponges were obtained from a local supermarket in Maha Sarakham (Thailand). Deionized water (18.2 MΩ·cm) was supplied by a RiOs Type I Simplicity 185 water purification system (Millipore, USA).

Table 3 Chemicals and reagent used in this work.

No.	Chemicals	Grade	Company
1	Sulfathiazole (STZ)	Analytical grade high-purity (>99%)	Sigma-Aldrich (Germany)
2	Sulfachloropyridazine (SCP)	Analytical grade high-purity (>99%)	Sigma-Aldrich (Germany)
3	Sulfamethoxazole (SMX)	Analytical grade high-purity (>99%)	Sigma-Aldrich (Germany)
4	Sulfadimethoxine (SDM)	Analytical grade high-purity (>99%)	Sigma-Aldrich (Germany)
5	Tetrabutylammonium bromide (TBABr)	Analytical grade	ACROS Organics USA
6	Dodecanoic acid	Analytical grade	Merck (Malaysia)
7	Hexanoic acid	Analytical grade	Merck (Malaysia)
8	Decanoic acid	Analytical grade	Merck (Darmstadt, Germany)
9	Octanol	Analytical grade	Merck (Darmstadt, Germany)

Table 3 Chemicals and reagent used in this work (continued).

No.	Chemicals	Grade	Company
10	Dodecanol	Analytical grade	Merck (Darmstadt, Germany)
11	Octanoic acid	Analytical grade	Merck (China)
12	Cetyltrimethylammonium bromide (CTAB)	Analytical grade	Merck (Darmstadt, Germany)
13	Sodium dodecyl sulfate (SDS)	Analytical grade	Merck (Darmstadt, Germany)
14	Triton X-114	Analytical grade	Merk (Darmstadt, Germany)
15	$Zn(NO_3)_2 \cdot 6H_2O$	Analytical grade	KemAus (Australia)
16	$Al(NO_3)_3 \cdot 9H_2O$	Analytical grade	KemAus (Australia)
17	$Ni(NO_3)_2 \cdot 6H_2O$	Analytical grade	KemAus (Australia)
18	$Mg(NO_3)_2 \cdot 6H_2O$	Analytical grade	Merck (Darmstadt, Germany)
19	Na_2CO_3	Analytical grade	Ajax Finechem (Australia)
20	NaOH	Analytical grade	Ajax Finechem (Australia)
21	Sodium alginate	Analytical grade	Loba chemie (India)
22	Acetonitrile	HPLC grade	Merck (Darmstadt, Germany)

Table 3 Chemicals and reagent used in this work (continued).

No.	Chemicals	Grade	Company
23	Methanol	HPLC grade	Merck (Darmstadt, Germany)
24	Ethanol	HPLC grade	Merck (Darmstadt, Germany)

Individual stock solution of STZ, SCP, SMX and SDM (1000 mg L^{-1}) was prepared in methanol (MeOH) and kept in a refrigerator (4 °C) until further use. A series of working standard solutions were diluted from the stocks with deionized water.

3.2 Instruments

3.2.1 HPLC-UV system

HPLC system used for the determination of the studied sulfonamides was a Waters 1525 Binary LC system (Waters USA) consisting of an in-line degasser, a Rheodyne injector with a 20-µL loop, and a Waters 2489 UV/Visible detector. To control and analyze chromatographic data, Empower 3 software was operated. The analytes separation was done by a reversed-phase Phenomenex Luna C18 (4.6 mm × 150 mm, 5 µm) (Phenomenex, USA) column with isocratic elution of mobile phase using 25 % acetonitrile in water at a flow rate of 1.0 mL min^{-1}. The detection wavelength was set at 270 nm.

3.2.2 UPLC-PDA system

UPLC system used for the determination of the studied sulfonamides was a UPLC ACQUITY H-class and photo diode array detector (Waters, USA). To control and analyze chromatographic data, Empower 3 software was operated. The analytes separation was done by a reversed-phase XSELEXT™ HSS C18 column (3.0 x 7.5 mm., 2.5 µm) (Waters, Ireland) column with isocratic elution of mobile phase using 25 % acetonitrile in water at a flow rate of 0.6 mL min^{-1}. The injection volume was 3 µL. The total time taken to detect all analytes were completed in 4 min. The detection wavelength was set at 270 nm.

3.2.3 Other instruments for characterization

Structural information of the investigated materials was obtained by Fourier transform infrared spectroscopy (FTIR) using a Bruker Invenio-S FT-IR (Bruker corp, Massachusetts, USA) and PerkinElmer® FT-IR model spectrum two (Waltham, Massachusetts, USA) using a diamond lens attenuated total resistance (ATR) with scan range of 4000–400 cm^{-1}. The X-ray diffraction (XRD) measurements of adsorbents before and after adsorption process was performed on an X-ray diffraction (XRD) (Model D8 Advance, Bruker, USA). N_2 adsorption-desorption analyses was evaluated using Brunner-Emmett-Teller (BET) (Micromeritics® TriStar II Plus (Georgia, USA)). Field-emission scanning electron microscope (FE-SEM) (SEM; TESCAN Model MIRA, UK) was used to visualize the morphologies of HDES-MS and LDHs@Alg beads and the thermal stabilities of the LDHs@Alg were investigated by TGA 4000 Thermogravimetric Analyzer (PerkinElmer, Inc., MA, USA). SPE was carried out using a 12-port Visiprep SPE vacuum manifold (Merck KGaA, Germany) coupled with Millipore Sigma$^{\text{TM}}$ pump (Thermo Fisher Scientific, USA) at a flow rate of 2.0 mL min^{-1}.

3.3 Water and honey samples

3.3.1 Water samples

The surface water samples were obtained from the different areas in Maha Sarakham province, Northeastern, Thailand.

3.3.2 Honey samples

The honey samples were purchased from local markets in Maha Sarakham province, Northeastern, Thailand.

3.4 Optimization of the proposed micro-SPE using melamine sponge impregnated hydrophobic deep eutectic solvents (HDES-MS) as sorbent

3.4.1 Preparation of hydrophobic deep eutectic solvents (HDES) and melamine sponge impregnated hydrophobic deep eutectic solvents (HDES-MS)

TBABr (as HBA) was mixed with long-chain fatty acid (as HBD) and heating at 60 °C under ultrasonic bath until the homogeneous solution was formed to obtain hydrophobic deep eutectic solvents. Six hydrophobic deep eutectic solvents were prepared (as listed in Table 4).

Table 4 Type of HDES

Type of HDES	Hydrogen bond acceptor (HBA)	Hydrogen bond donors (HBD)	Mole ratio
HDES1	TBABr	Decanoic acid	1:3
HDES2		Dodecanoic acid	
HDES3		Octanoic acid	
HDES4		Dodecanol	
HDES5		Hexanoic acid	
HDES6		Octanol	

A melamine sponge (MS) was firstly cut to cubic size of 0.7x0.7x0.7 cm^3. Then, the MS washed with DI water and ethanol and then left to dry. The MS (1 piece) was then impregnated by dropping 100 µL of the as-prepared hydrophobic deep eutectic solvents into MS. The MS impregnated hydrophobic deep eutectic solvents (HDES-MS) were frozen at -4 °C for 30 min.

3.4.2 Micro-SPE

The micro-SPE procedure is illustrated in Figure 2. The melamine sponge impregnated hydrophobic deep eutectic solvent sorbent (1 piece) was placed into the SPE cartridge. CTAB 0.03 M (150 µL) was added into standard/sample solution and then adjusted to 10 mL in volumetric flask by water. After that the solution was flowed through the as-prepared material using Millipore Sigma^{TM} pump at a flow rate of 2 mL min^{-1}. In this step, sulfonamide-CTAB was adsorbed in melamine sponge impregnated hydrophobic deep eutectic solvents sorbent. The hydrophobic interactions between hydrophobic tail of surfactant and hydrophobic sites of HDES2-MS while the hydrophilic parts of surfactant interacted with the sulfonamide in aqueous phase which allowed to enhance the adsorption efficiency. The analyte in the sorbent was then desorbed with 500 µL of methanol by vacuum manifold. Before determination step, the eluate was sonicated at 60 ºC for 10 minutes and the eluate phase (20 µL) was injected into HPLC-UV system.

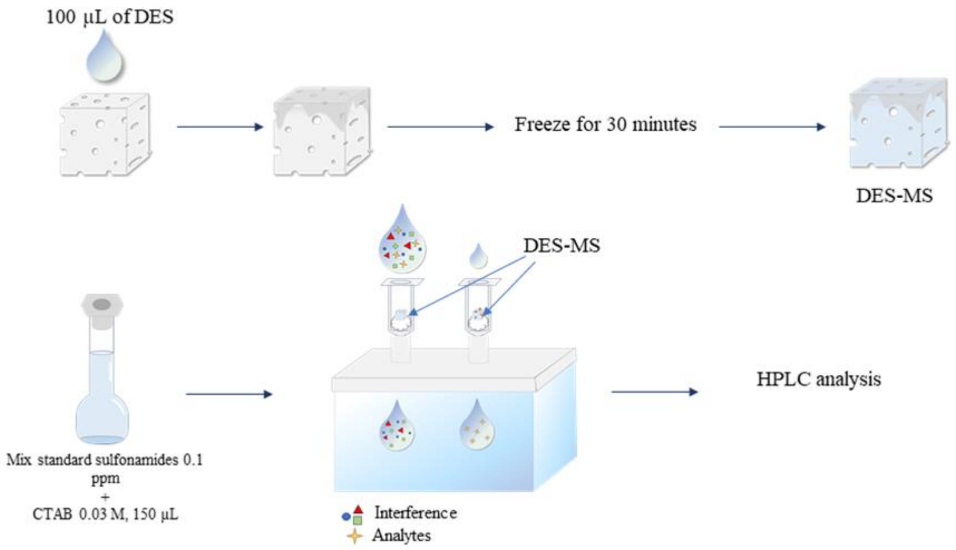


Figure 2 Schematic diagram of the proposed micro-SPE procedure for determination of sulfonamides.

The experimental parameters affected the extraction efficiency were studied.

3.4.2.1 Effect of type of hydrogen bond donor to HDES formation

Precursors of HDES are usually chosen considering their solubility in an aqueous phase, melting point of the resulted eutectic mixture and extraction properties [78]. The main idea of this presented work was to find the precursors that change their switchable state when temperature was changed. To use this feature for impregnated on melmine sponge as adsorbent to enhance the extraction performance. Accordingly, in this work HDES formation used TBABr (HBA)-based with different genre of alcohol and fatty acid (HBD) namely decanoic acid, dodecanoic acid, octanoic acid, hexanoic acid, dodecanol and octanol were studied.

3.4.2.2 Effect of mole ratios and volume of HDES formation

The mole ratios of optimal HDES formation were studied by TBABr was fixed at 1 mole and the optimal HBD was changed in the range of 1 to 4 mole. In addition, the appropriate amount of DES also affects the analysis of analytes. Therefore, in this work, the appropriate volume of DES was studied in the range of 50 to 200 µL.

3.4.2.3 Effect of size of melamine sponges

The melamine sponges were tested with disparate cubic size of melamine sponge namely 0.3, 0.5, 0.7 and 1.0 cm^3.

3.4.2.4 Effect of type and amount of surfactant

Surfactants are one of important parameter should be studied. Because the use of surfactants can increase extraction efficiency by improving solubility, increasing selectivity, and reducing organic solvent consumption [117]. Thus, in the presented work, the different kind of surfactants were literated viz without surfactant addition, cetyltrimethylammonium bromide (CTAB), sodium dodecyl sulfate (SDS), and Triton X-114. Moreover, in this studied, the concentration of selected surfactant was investigated.

3.4.2.5 Effect of type and volume of desorption solvent

The desorption solvents were tested that is DI water, ethanol, methanol and acetonitrile. The selected desorption solvent was varied in the range 200 to 600 µL.

3.4.2.6 Reusability of adsorbent

The reusability of HDES-MS as sorbent for extraction sulfonamide antibiotics was investigated. After adsorption and desorption process. In order to ensure elimination of residues on the sorbent before extraction new cycle using the proposed method, the adsorbent was washed with methanol 5 mL and dried.

3.4.2.7 Preparation of samples

The water samples were taken from different areas located in northeastern, Thailand. These samples were filtered through a Whatman filter No. 1. Then, the filtrate was filtered through a 0.45 µm nylon membrane filter.

3.5 Optimization of the proposed micro-SPE using layered double hydroxide combined with alginate as adsorbent

3.5.1 Preparation of layered double hydroxide combined with alginate beads formation (LDHs@Alg beads)

LDHs composite was fabricated via co-precipitation technique (type of LDHs was shown in Table 5). Initially, the respective metal nitrate solutions were prepared by dissolving 0.01 mol L^{-1} of $Mg(NO_3)_2{\cdot}6H_2O$ and $Al(NO_3)_3{\cdot}9H_2O$ were dissolved in 100 mL DI water (salt solution). While, 100 mL of 0.1 mol L^{-1} NaOH and Na_2CO_3 were added dropwise to the salt solution. The precipitate was occurred. After dripping step, the solution was put in an oil bath heated to 85ºC under magnetically stirred for 6 hours. Next step, the precipitate was separated by centrifugation and dried it at 60 ºC until dry. Finally, LDHs was synthesized. The scheme of LHDs synthesis was shown in Figure 3.

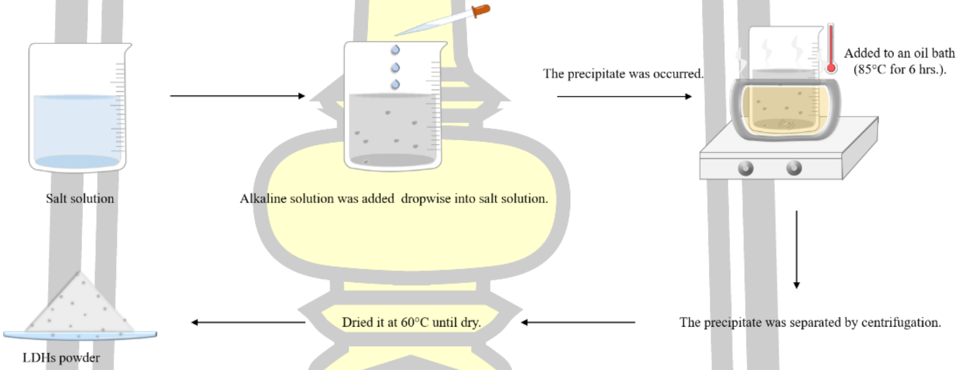


Figure 3 Schematic diagram of LDHs synthesis.

Table 5 Type of LDHs

Type of LDHs	LDH	Molar ratios
Type 1	Zn-Al LDH	1:2
Type 2	Mg-Al LDH	1:2
Type 3	Ni-Al LDH	1:2

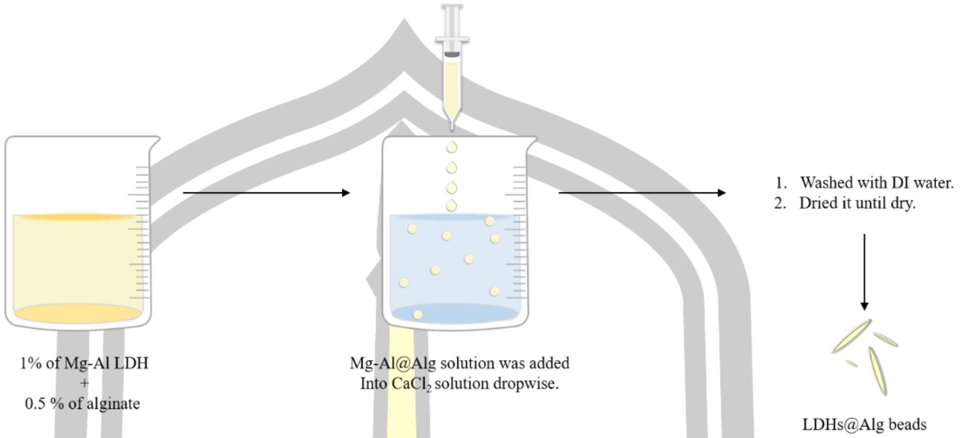


Figure 4 Schematic diagram of LDHs@Alg beads formation

3.5.2 LDHs combined with alginate beads (LDHs@Alg beads) formation

In briefly, 1 g of synthesized LDHs was dispersed in 100 mL of DI water. Thereafter, 0.5 g of sodium alginate was added into solution under constant and severe mechanical stirring till homogeneous solution was achieved. While 0.2 M of $CaCl_2$ solution was prepared. Subsequently, the homogenous solution was dropped in to $CaCl_2$ solution dropwise by syringe. The resultant of LDHs@Alg beads were washed with DI water to eliminate unreacted substances. The prepared beads were dried at room temperature until dry. The dried synthesized materials were stored in desiccator until use. The beads formation was shown in Figure 4.

3.5.3 Micro-SPE

For micro-SPE is an easy-to-do procedure (As shown in Figure 5). Firstly, LDHs@Alg as adsorbent was transferred into syringe with cotton underneath followed by conditioning step with methanol and DI water 5 mL for each solvent. Then, a 0.1 mg L^{-1} of sulfonamide standard solution or sample containing CTAB was prepared and transferred it through adsorbent. Next step, the adsorbent was eluted by acetonitrile. Thereafter, the eluate was filtered through 0.22 µm nylon membrane filter. Finally, 3 µL of it was injected to UPLC-PDA for sulfonamide antibiotics analysis.

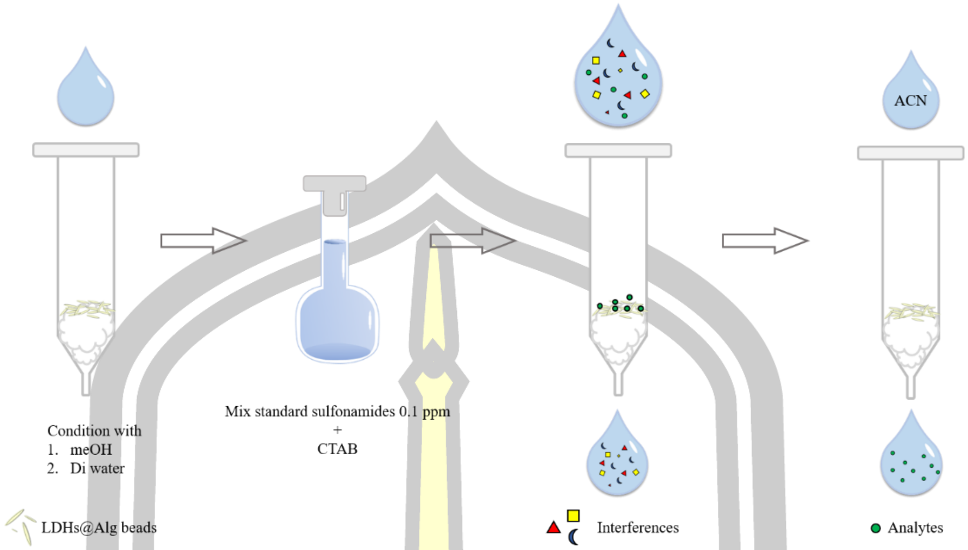


Figure 5 Schematic diagram of micro-SPE procedure.

The experimental parameters affected the extraction efficiency were studied.

3.5.3.1 Effect of LDHs synthesis

In present work three types of 1:2 ratios of LDH were varied namely, Zn-Al LDH, Mg-Al LDH and Ni-Al, and the different ratio of selected M^{2+} to M^{3+} species in the metal layers were studied.

3.5.3.2 Effect of proportion of sodium alginate for beads formation

The 1% w/v of prepared LDHs was defined and different of amount sodium alginate were studied in the range 0.5 to 3 %w/v.

3.5.3.3 Effect of amount of beads

The amount of adsorbent was varied to achieved high adsorption performance. The studied condition was studied from 0.01 to 0.50 g.

3.5.3.4 Effect of surfactant

In the present work was studied with three various kinds of surfactant with different charge consisting of CTAB, SDS and Triton X-114, respectively. Then, the chosen surfactant was studied with different concentration.

3.5.3.5 Effect of desorption solvent

The present work, four desorption solvents were varied, consisting of DI water, acetonitrile, methanol and ethanol followed by effect of volume of selected desorption solvent studied. The volume of desorption solvent was estimated from 500 to 1000 μL.

3.5.3.6 Reusability

The reusability of Mg-Al@Alg beads as sorbent for extraction sulfonamide antibiotics was investigated. After adsorption and desorption process. In order to ensure elimination of residues on the sorbent before extraction new cycle using the proposed method, the adsorbent was washed with acetonitrile 5 mL for two times and dried.

3.5.3.7 Sample preparation

The honey samples were taken from different local markets located in northeastern, Thailand. These samples were weighted about 5 g and diluted to 50 mL in volumetric flask. Then the solution was filtered through a Whatman filter No. 1. Then, the filtrate was filtered through a 0.22 µm nylon membrane filter.

3.6 Statistical analysis

Results were obtained from three replicate experiments, with the mean ($\bar{X}$), standard deviation (SD) and relative standard deviation (%RSD) determined using OriginPro 2018 (OriginLab Software, Northampton, MA, USA) and Microsoft Excel. The p values < 0.05 were considered significant. In all graphs, a linear regression analysis and %RSD were conducted using Microsoft Excel 2019 software. All chromatograms were calculated and plot by OriginPro 2018.

3.7 Evaluation of enrichment factor (EF), matrix effect (ME), percentage relative recovery (RR, %) and adsorption capacity

The enrichment factor (EF) was calculated using Eq. (1).

$$EF = S_{ex} / S_0 \qquad (1)$$

where S_{ex} and S_0 are the slopes of the calibration graph with and without extraction, respectively.

The ME is estimated by the ratio of the slope of the calibration curve in the matrix to that in the solvent, according to Eq. (2):

$$ME(\%) = \frac{S_m}{S_S} \times 100 \qquad (2)$$

where S_m and S_s illustrate the slopes of the calibration curve in the matrix and solvent, respectively.

The percentage relative recovery (RR, %) was calculated as the % amount of analyte recovered from matrix with reference to the extracted standard (standard spiked into the same matrix), according to the following Eq. (3):

$$\text{RR (\%)} = \frac{C_{found} - C_{real}}{C_{added}} \times 100 \qquad (3)$$

Where C_{found} is the concentration of analyte after adding a known amount of working standard to real sample, C_{real} is the analyte concentration in real sample, and C_{added} represents to the concentration of a known amount of working standard that was spiked into the real samples.

The adsorption capacity was calculated as the maximum adsorb analytes in adsorbent [118], according to the following Eq. (4):

$$\text{Adsorption capacity} = \frac{C_0 \text{ x } V_E}{m} \qquad (4)$$

Where C_0 (mg L^{-1}) is the studied concentration, V_E (mL) is the maximum volume of sulfonamides solution passed through without self-elution and m (g) is amount of adsorbent.

CHAPTER IV
RESULTS AND DISCUSSION

4.1 Evaluation results of characterization optimization and others of micro-SPE procedure using HDES-MS as adsorbent

4.1.1 Characterization of hydrophobic deep eutectic solvents (HDES) and melamine sponge impregnated hydrophobic deep eutectic solvents (HDES-MS)

In order to establish the construction and structure of the studied HDES and HDES-MS, several techniques were used including Fourier Transform Infrared Spectroscopy (FTIR), scanning electron microscope (SEM), X-ray diffraction (XRD) and Brunauer–Emmett–Teller theory (BET).

FTIR spectra (as shown in Figure 6) of each solvent i.e. TBABr (as shown in Figure 6(a)), dodecanoic acid (as shown in Figure 6(b)), and HDES2-MS (as shown in Figure 6(c)) were determined. The FTIR spectrum shows that the DES peak on MS (as shown in Figure 6(c)) is similar to substances used to synthesis DES (as shown in Figure 6(a) and (b)). The characteristics were found to be similarly, such as C-H stretch (~2484.42 to 2915.56 cm $^{-1}$) and a long-chain band about 736.77 cm $^{-1}$. These peaks demonstrated that C-H exists on dodecanoic acid and TBABr, there were bonded in a long chain. Moreover, C=O stretch (1695.87 cm $^{-1}$), C-O stretch (1301.32 cm $^{-1}$), and O-H bend (935.65 cm $^{-1}$) were indicated that the -COOH group were observed in the structure. In addition, C-N stretch (~ 1165.90 cm $^{-1}$) indicated that C atoms and N atoms are bonded together on the TBABr structure. The broad bands between 3500 and 3000 cm $^{-1}$ were assigned to the O–H stretching vibration of pure fatty acids. Due to the construction of hydrogen bonding between bromide anion in TBABr and hydroxyl group in fatty acids, consequently, their vibrational intensities were decreased. All peaks were ascribed to the original components (TBABr and fatty acids) and no further peaks were observed, indicating no reactions and dissociation of the precursors during the formation of DESs [37]. Therefore, it can be confirmed that all prepared DESs were synthesized successfully.

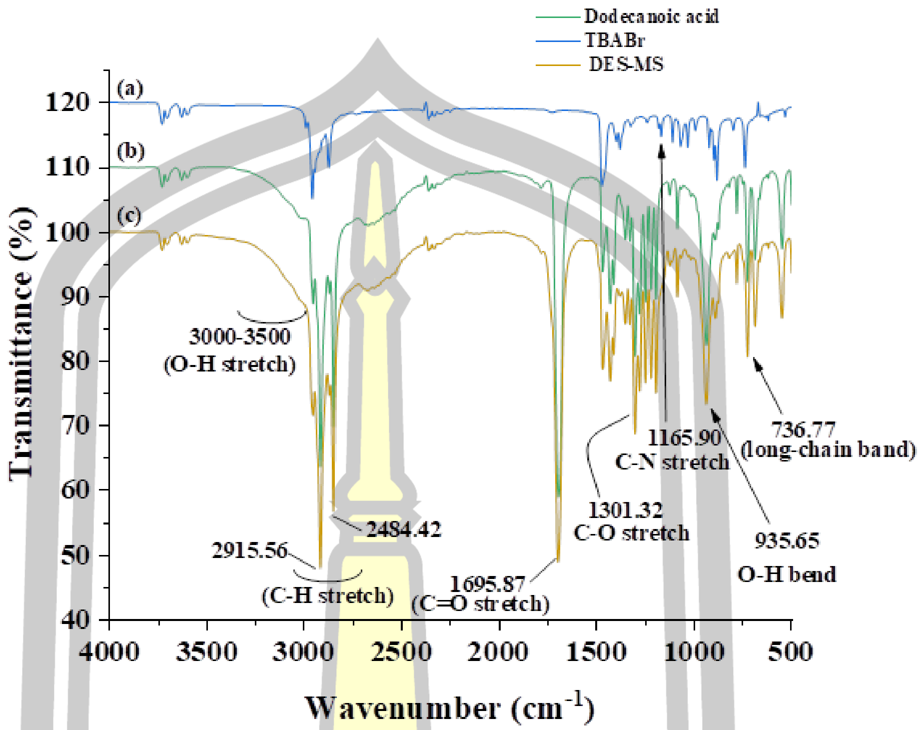


Figure 6 FT-IR spectra of TBABr (a), dodecanoic acid (b) and HDES-MS (c).

In addition, SEM images of pure MS and HDES2-MS are displayed in Figure 7, showing that pure MS is highly porous with melamine wires interconnected to form a 3D porous structure [119]. The pores are relatively uniform ranging between 100 µm and 200 µm and the surface of framework was very smooth [120]. After coating, those pores of MS are penetrated with HDES2 and the surfaces are covered as shown in Figure 7b. The MS wires still kept their original porous structures without collapse. After adsorption process (as shown in Figure 7c), the MS sites could be exposed to sulfonamides. After going through the desorption process (as shown in Figure 7d), it was found that the free space of DES-MS increased because HDES-sulfonamides were eluted from the MS.

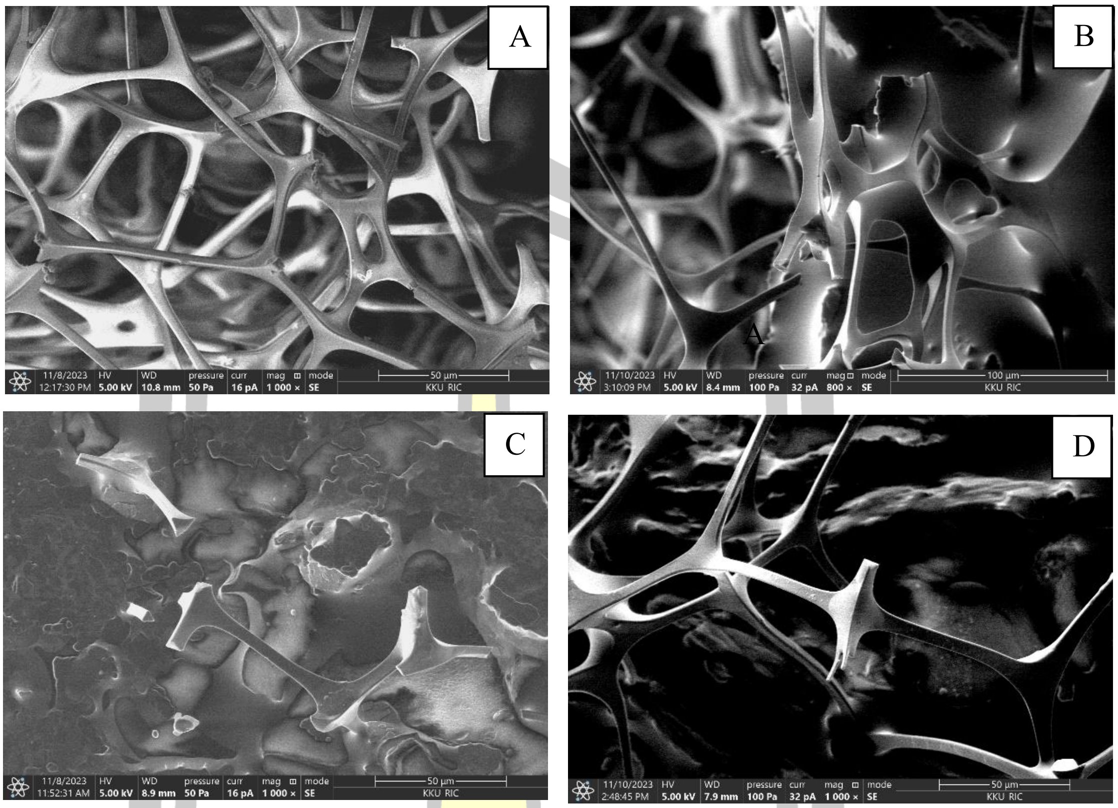


Figure 7 Morphologies of HDES-MS as adsorbent to preconcentration of SA; A to D are SEM images of pure sponge (A), HDES-MS (B), HDES-MS adsorption (C) and HDES-MS desorption (D).

X-ray diffraction (XRD) pattern was used to examine the crystalline structure of HDES2-MS. The measurement data were collected in a range of $2\theta = 5–80°$ by a scanning rate of 0.04° min^{-1} at room temperature. The XRD results of pure MS and HDES2-MS are shown in Figure 8. The XRD pattern of the pure MS is a broad, indicating that is amorphous solid. After HDES2 was added, the major XRD peaks of HDES2 are found at 2θ = 2°, 10.5°, 22° and 24.5° which indicated that these substances are crystalline solids. These indicate that the HDES2 phase was formed in the MS.

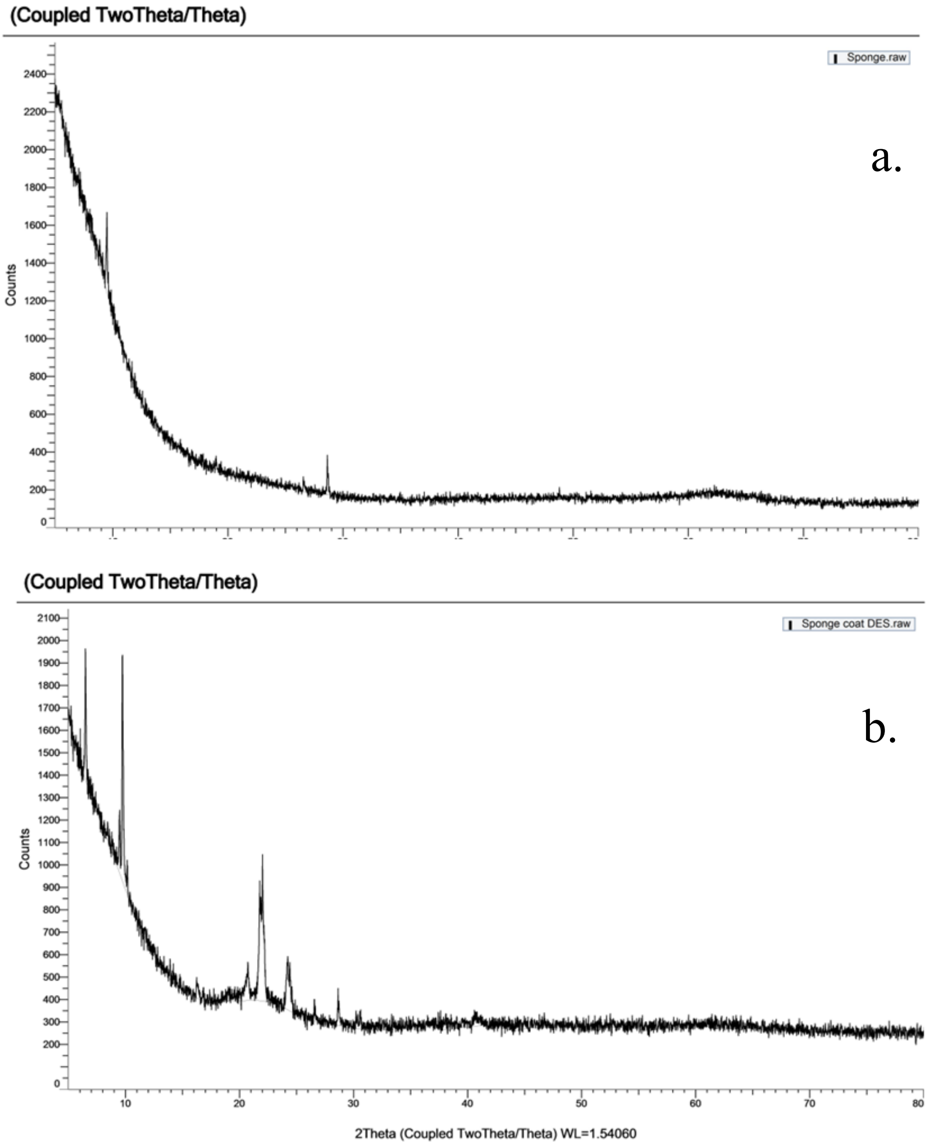


Figure 8 XRD pattern of (a) melamine sponge and (b) sponge impregnated with DES (DES-MS).

Surface area and porosity are two important physical properties which used to determine the capacity of the materials. BET (Brunauer, Emmett, and Teller) determinations with nitrogen N_2 as adsorbate, was used to determine the surface area and porosity of the MS. Obviously, MS showed Type-III adsorption in the IUPAC classification (as shown in Figure 9), illustrating that MS has a large pore size with weak interaction. This type occurs where the adsorbate–adsorbate interaction is big compared to adsorbate–sorbent interaction. The surface area of MS was up to 13.3773

m^2 g^{-1} and pore diameter 85.298 Å. After modification, the lower porosity of HDES-MS results from the uneven distribution of the eutectic solvents on the MS surface [29]. The result indicated that HDES obstructed the pores of MS, resulting in a preconcentration of sulfonamides.

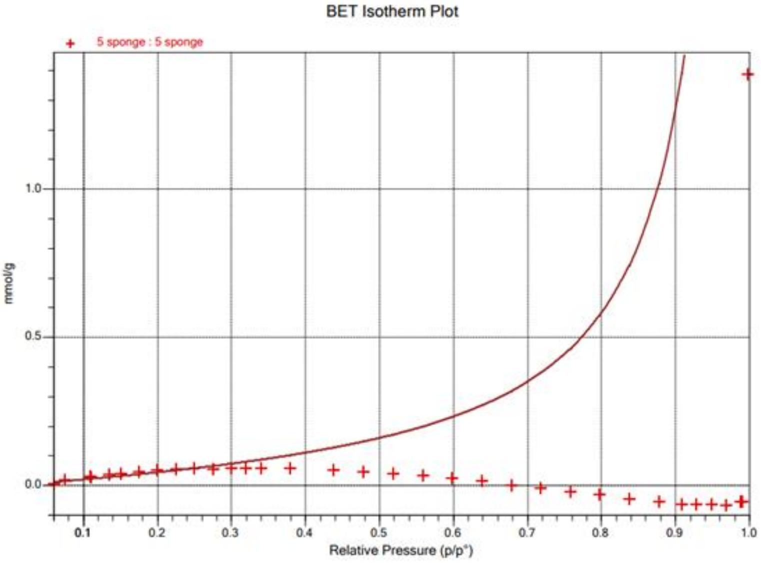


Figure 9 N_2 adsorption-desorption isotherms of MS.

4.1.2 Optimization of micro-SPE using HDES-MS as sorbent

In the process of optimization experiments, aqueous standard solutions containing 100 µg L^{-1} of each sulfonamide were investigated using the univariate method (which is the one-variable-at-a-time (OVAT) approach, where only one factor at a time is varied and optimized [4]. Various parameters were studied including HDES composition (TBABr: Decanoic acid, TBABr:Dodecanoic acid, TBABr:Octanoic acid, TBABr:Dodecanol, TBABr:Hexanoic acid and TBABr: Octanol) at molar ratio of 1:3, mole ratios of HDES (1:1, 1:2, 1:3 and 1:4), cubic sizes of sponge (0.3x0.3x0.3, 0.5x0.5x0.5, 0.7x0.7x0.7 and 1.0x1.0x1.0 cm^3), kind of surfactants (cetyltrimethylammonium bromide, sodium dodecyl sulfate and Triton X-114), concentrations of CTAB (0.01, 0.03, 0.05, 0.07 and 0.10 M), kind of desorption solvent (acetonitrile, methanol, ethanol, and water) and volume of desorption solvent (200, 300, 400, 500 and 600 µL).

4.1.2.1 Type of HDES

Lately, the application of ammonium and phosphonium salts based-DES have been literate with respect to their physiochemical properties together with their aromatic extraction. It was apprized that the halide based quaternary ammonium and phosphonium salts easily mixed with HBD to form DES, which were found to be greatly selective for aromatic compounds [121]. However, recently, some reported that quaternary ammonium-based salt DES had much lower viscosities than phosphonium-based salt DES [122]. To prevent the viscosity problem while analysis process. Therefore, quaternary ammonium salt was interested as HBA. In addition, recently one frequently used HBA-based quaternary ammonium salts is tetrabutylammonium bromide (TBABr). It can be formed along with various HBD for analytical chemistry purposes [123]. Moreover, TBABr-based HDES have been used for analysis of several kinds of samples, such as water, food and drugs, using several techniques followed by HPLC-UV/FLD detection, UV–Vis spectrophotometric quantification[123]. With these great features. In this work TBABr was used as optimum HBA along with six types different HBD. This has allowed the creation of six HDES consist of the combination of a HBA (ammonium salt) and HBD.

The composition of HDES solvents is important for electrostatic interaction, selectivity, and efficient separation with the analyte [124]. Furthermore, hydrogen bond strength between the DES components and cation symmetry are key peculiarities in DES synthesis. The most essential freezing point depressions are observed in those mixtures where the DES components have a more supereminent ability to form hydrogen bonds and a lower cation symmetry [125]. Thus, for the preparation of the DES, TBABr was chosen as the HBA for its cation's symmetrical structure [126]**.** Different HDES components (as shown in Table 4) were generated using TBABr and different fatty acid/alcohol at molar ratio of 1:4. The results in Figure 10 showed that the extraction efficiency increased with increasing the length of hydrocarbon chain (from C7 to C12). The highest extraction efficiency for the studied sulfonamides, was achieved when HDES4 (a mixture of TBABr and dodecanol) was used. Because of the long chain length of the two HBA and HBD components led to the lower solubility of these systems in water (The solubility of the dodecanol in water is approximately 0.004 g L^{-1}). However, high viscosity of the eluate with bad chromatographic signal were obtained. For this result, HDES2 (a mixture of TBABr and dodecanic acid) was chosen for subsequent studies. The solubility of the dodecanoic acid in water is approximately 0.055 g L^{-1}at 20 °C). Moreover, a strong affinity between the HDES and sulfonamides can be obtained. The extraction can proceed through hydrogen bond, hydrophobic and electrostatic interactions with fatty acid [127]. In addition, there are hydrogen bond formation with aliphatic amine and carboxyl group of fatty acids. The possible adsorption mechanism between the analytes and HDES and HDES formation mechanism as shown in Figure 11.

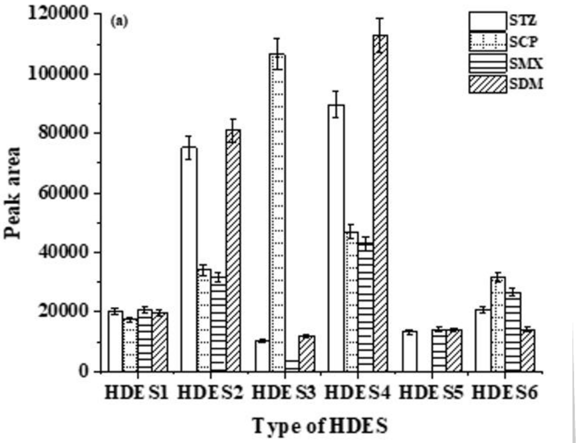


Figure 10 Effect of type of HDES. Error bars represent the standard error (n = 3).

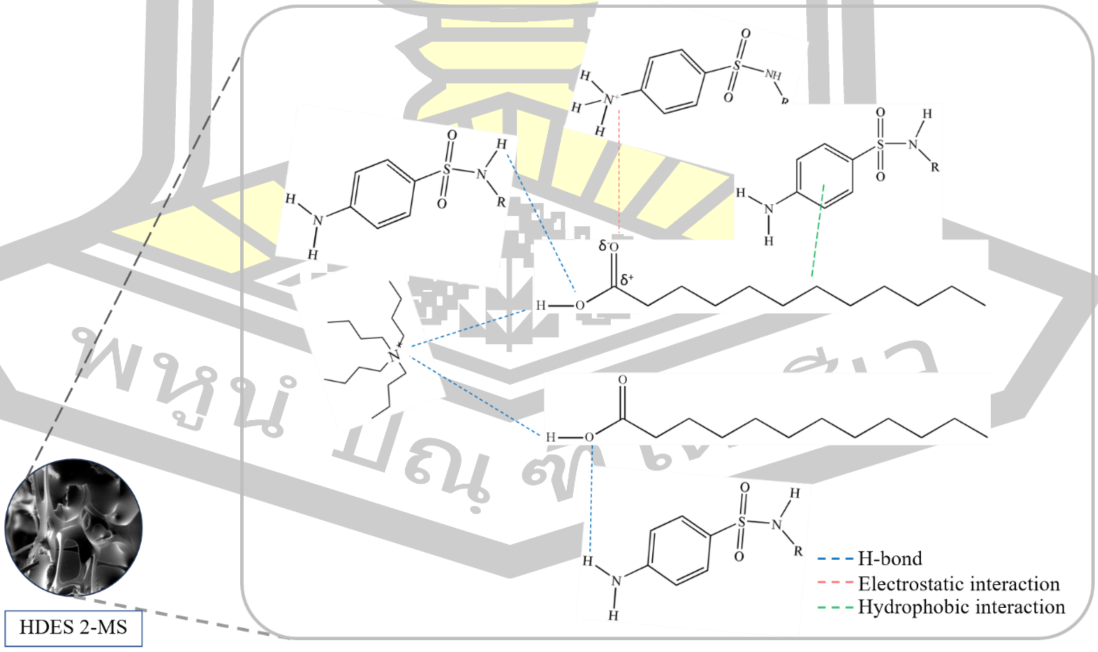


Figure 11 The possible adsorption interaction of analytes and HDES.

3.4.2.2 Amount of selected HDES

The mole ratios of TBABr to dodecanoic acid were then studied by varying the ratios from 1:1 to 1:4, resulted shown in Figure 12(a). The results revealed that the mole ratios of at 1:4 provided the highest extraction efficiency due to a large number of hydrophobic sites. When the mole ratios of TBABr to dodecanoic acid at 1:5 therefore the viscosity increased, resulting in the HPLC pressure increased. Hence, mole ratios of TBABr to dodecanoic acid (HDES2) at 1:4 was chosen. Moreover, volumes of HDES2 were studied (50, 100, 150, and 200 μL). The results in Figure 12(b) exhibit that the extraction efficiency increased with the volume of HDES2 from 50 to 100 μL and then decreased due to the dilution effect. Therefore, 100 μL of HDES2 was used for the subsequent experiment due to it is acceptable for extraction of the analytes at the concentration test.

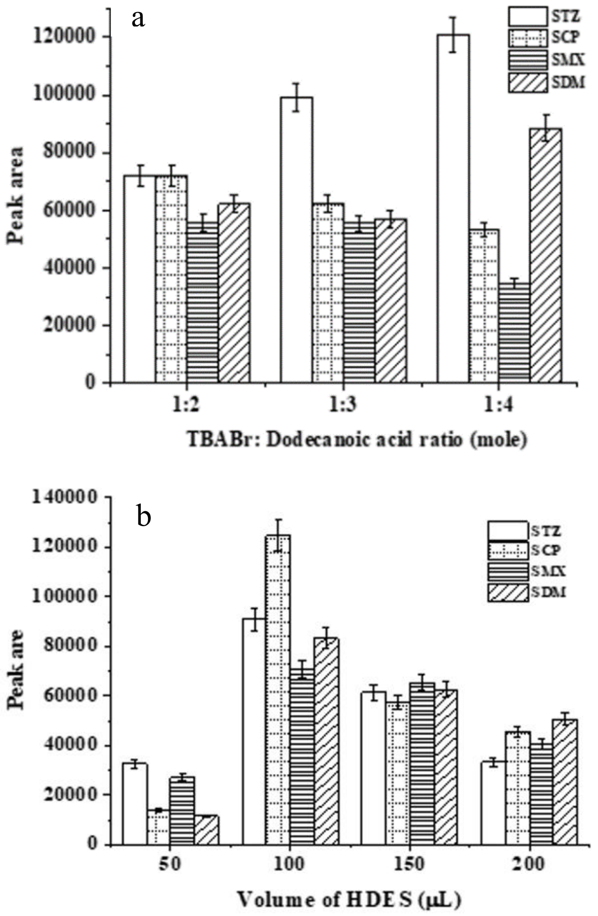


Figure 12 Effect of (a)TBABr: Dodecanoic acid ratio (mole) and (b) volume of HDES. Error bars represent the standard error (n = 3).

4.1.2.3 Sizes of melamine sponge

To eradicate the used of other agitator for phase separation, the MS impregnated DES through hydrophobic interaction was used as a supporter [36]. In this work, commercially available melamine sponges were cut into a cuboid following previous work [27,81] with the modification of the size. Four sizes of sponge were studied including 0.3x0.3x0.3, 0.5x0.5x0.5, 0.7x0.7x0.7 and 1.0x1.0x1.0 cm^3 (as shown in Figure 13). The extraction efficiency was gradually increased from 0.3x0.3x0.3 to 0.7x0.7x0.7 cm^3, and then decreased due to the uneven distribution of the eutectic solvents on the MS surface. Therefore, 0.7x0.7x0.7 cm^3 of melamine sponge was selected.

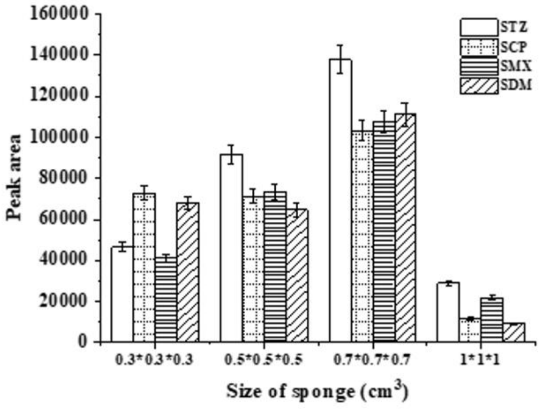


Figure 13 Effect of size of sponge (cm^3). Error bars represent the standard error (n = 3).

4.1.2.4 Type of surfactants

To increase the mass transfer of analytes from the aqueous to the organic phase as a result the extraction efficiency inceased, therefore surfactant was added [129]. Generally, surfactant molecule consists of two parts including hydrophilic head and hydrophobic tail. To measure the degree of their hydrophilicity or lipophilicity, various surfactants with different hydrophilic-lipophilic balance (HLB) values, were studied [1]. HLB values were evaluated by Davies' method which based on chemical groups of molecules [130]. HLB values can be calculated by the balance of the size and strength of the hydrophilic and lipophilic moieties of a surfactant molecule. Surfactants with lower HLB values are more hydrophobic. Various kind of surfactants with different HLB value were investigated including cationic surfactants (cetyltrimethylammonium bromide (CTAB), HLB = 7.3), anionic surfactants (sodium dodecyl sulfate (SDS), HLB = 40.0), and non-ionic surfactants: Triton X-114, HLB = 12.4) [1]. And the results are presented in Figure 14, it revealed that the peak areas of the four representative sulfonamides gradually increased with the addition of CTAB. Due to the low HLB value of CTAB contributed their high hydrophobic interactions between hydrophobic tail of surfactant and hydrophobic sites of HDES2-MS. In addition, the hydrophilic parts of surfactant interacted with the sulfonamides in aqueous phase. Therefore, the addition of CTAB was chosen for further studied.

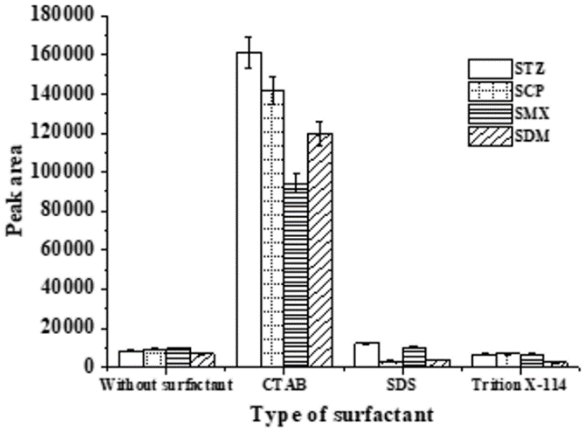


Figure 14 Effect type of surfactant. Error bars represent the standard error (n = 3).

4.1.2.5 Concentration of selected surfactant

Different concentrations of CTAB were examined in the range of 0.01–0.10 M. The results are shown in Figure 15. The peak areas of all the analytes slightly increased with increasing in CTAB concentration up to 0.03 M, then slightly decreased. When the concentration of surfactant increased therefore the viscosity increase, as a result the detection decreased of target substances [11]. Thus, CTAB 0.03 M was added for further studied.

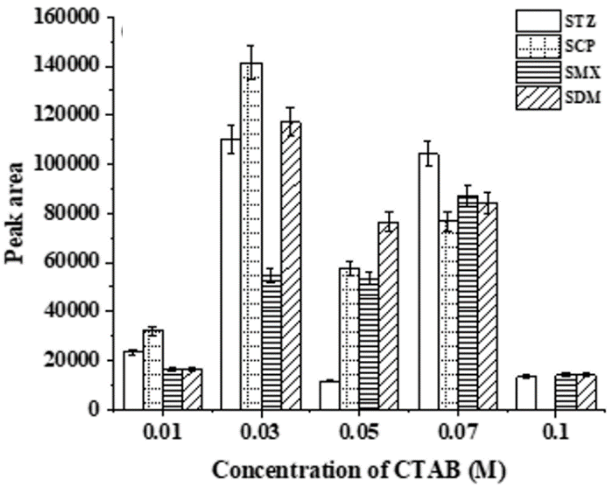


Figure 15 Effect concentration of CTAB. Error bars represent the standard error (n = 3).

4.1.2.6 Type of desorption solvents

In the extraction process, to desorb the analytes from the sorbent is an important step [86]. Due to the polarity of the target analytes, four desorption solvents were studied, including acetonitrile, methanol, ethanol, and water. As shown in Figure 16, methanol provides the highest desorption power for the studied SCP and SDM while acetonitrile grants the highest desorption power for the studied STZ and SMX. However, bad chromatogram was obtained when acetonitrile was used as desorption solvent. Therefore, methanol was selected for further studied.

The effect of methanol (as desorption solvent) volume was examined in the range of 200–600 µL. It was found that the extraction efficiency slightly increased with increasing the volume of desorption solvent up to 500 µL (data not shown). On the contrary, the use of relatively higher desorption solvent volume would reach to increase solubility of analytes and the analytical signals decrease by increasing the extraction solvent volume due to dilution effect. Therefore, the analytes were desorbed using 500 µL of MeOH for further experiments.

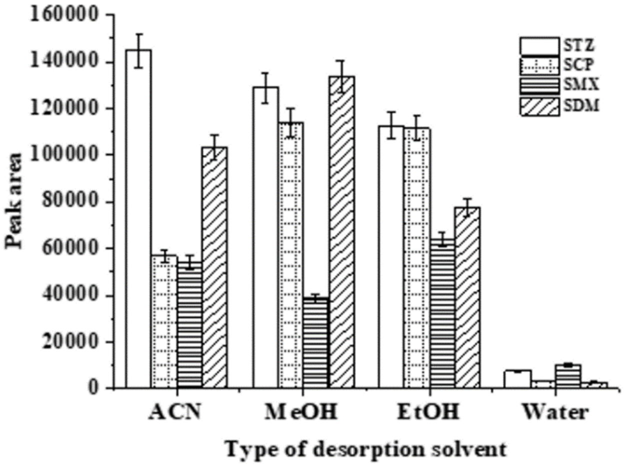


Figure 16 Effect of type of desorption solvent on the extraction efficiency. Error bars represent the standard error (n = 3).

The optimal synthesis and extraction conditions for the investigated method, were standard/sample solution (10 mL), 0.7x0.7x0.7 cm^3 of cubic MS, 100 µL of HDES2, 0.03 M CTAB (150 µL), and 500 µL methanol (as desorption solvent). The optimum conditions of mico-SPE for sulfonamide antibiotics analysis are summarized in Table 6.

Table 6 The optimum conditions of micro-SPE for sulfonamide antibiotics analysis.

Extraction process	Extraction condition
HDES	TBABr: dodecanoic acid (1: 4 mol ratios), 100 µL
Sizes of melamine sponge	Cubic 0.7x0.7x0.7 cm^3
Surfactant	CTAB 0.03 M, 150 µL
Desorption solvent	MeOH, 500 µL

4.1.3 Stability and reusability

To assess the stability of HDES2-MS which evaluated in terms of reproducibility of the production procedures for studied sulfonamides across six different batches. The percentage of RSD were calculated (data not shown), the findings show high accuracy, with RSDs less than 8.1%. These favorable results indicate that the suggested HDES2-MS sorbent can be used to extract all the sulfonamides under optimization.

In order to showed an excellent greenness characteristic of the current method, good reusability of the as-prepared materials is an important characteristic. The number of times the sorbent material can be reused is an important factor, as well as the economics of the process [1]. The reusability of HDES2-MS was investigated (data not shown). In this study, methanol was used to desorb sulfonamides from HDES2-MS. After the first cycle of adsorption and desorption, the HDES2-MS was washed by methanol and then dried before applying a new micro-SPE cycle. The results indicated that the efficiency of the sorbent gradually decreased, being reusable for up to three times. After that, the signal decreased due to DES diffused into the aqueous phase. Furthermore, this developed method exhibited better reusability than commercial SPE sorbents, as most commercial sorbents cannot be reused after the extraction [131].

4.1.4 Analytical features of the developed method

The analytical figures of the developed method for the extraction of sulfonamides using as prepared material are summarized in Table 8. The linearity of the proposed method was evaluated by the analysis of working standard solutions of sulfonamides at nine different concentrations within the working range. Each concentration was injected three times. The method exhibited good linearities were achieved in the concentration range from 30 to 1000 µg L^{-1} for sulfathiazole (STZ), from 10 to 1000 µg L^{-1} for sulfachloropyridazine (SCP) and sulfamethoxazole (SMX) and from 100 to 3000 µg L^{-1} for sulfadimethoxine (SDM) with R^2 more than 0.99. The LOQs and LODs were evaluated based on a signal-to-noise ratios and were based on analytical responses of 10 [132] and three times the background noise, respectively. LODs range from 0.64 to 7.5 µg L^{-1} and LOQs range from 1.92 to 22.5 µg L^{-1}. Good reproducibility (n = 5, %RSD ≤ 5.0) and precision (n = 3 × 5, %RSD < 5.0) were also obtained. The enrichment factors (EF) were calculated by comparing the slopes of the calibration graphs obtained by proposed method and direct HPLC. The analytical performances of sulfonamide determination by direct HPLC were shown in Table 7. The compared slope were found to be in the range of 4.00–5.33. The precision in term of intraday (n =5) and over several days (n = 5 × 3 days) were also investigated as the RSDs of retention time (t_R) and peak area of the studied compounds. High precisions were observed with RSD lower than 2.67 (t_R) and 4.83 (peak area), respectively. The chromatograms of the standard sulfonamides obtained from direct HPLC and micro-SPE-HPLC process are presented in Figure 17.

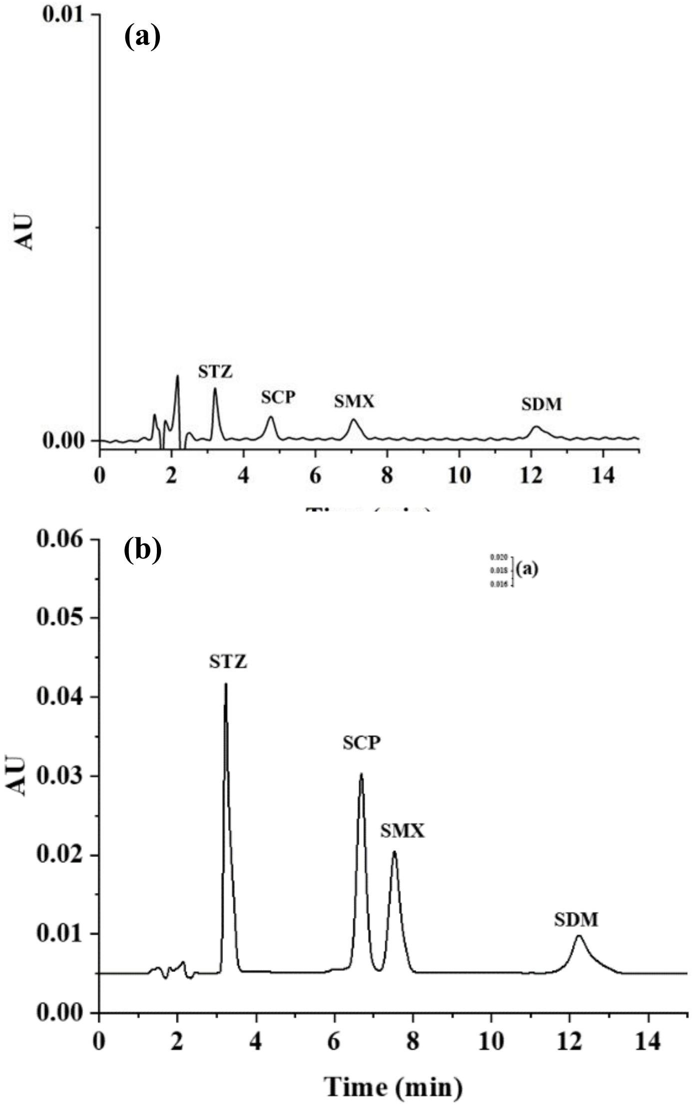


Figure 17 Chromatograms of the studied sulfonamides obtained by (a) direct HPLC and (b) the proposed micro-SPE method.

Table 7 Analytical performance of four sulfonamides by direct HPLC

Analyte	**Linear range ($\mu g\ L^{-1}$)**	**Linear equation**	**R^2**	**LOD ($\mu g\ L^{-1}$)**	**LOQ ($\mu g\ L^{-1}$)**	**Intra-day[a] precision (n=5), RSD (%)**		**Inter-day precision (n=3 × 5), RSD (%)**	
						t_R	**Peak area**	**t_R**	**Peak area**
Sulfathiazole	90 – 3000	y = 114090x + 2188	0.9995	3.00	9.00	0.47	2.78	0.61	2.38
Sulfamethazine	30 – 3000	y = 115712x + 7970.2	0.9953	10.0	30.0	0.41	2.20	0.42	2.95
Sulfamethoxazole	30 – 3000	y = 108579x + 259.84	0.9999	10.0	30.0	2.59	1.58	1.85	4.02
Sulfadimethoxine	90 – 3000	y = 120897x - 1581.8	0.9999	30.0	90.0	1.64	1.97	1.33	1.81

[a] Precision were investigated at the concentration of 300 $\mu g\ L^{-1}$

Table 8 Analytical performance of the proposed method for determination of sulfonamide residues.

Analyte	**Linear range ($\mu g\ L^{-1}$)**	**Linear equation**	**R^2**	**LOD ($\mu g\ L^{-1}$)**	**LOQ ($\mu g\ L^{-1}$)**	**Intra-day[a] precision (n=5), RSD (%)**		**Inter-day precision (n=3 × 5), RSD (%)**		**EF (C_{ex}/C_0)**
						t_R	**Peak Area**	**t_R**	**Peak area**	
STZ	30-1000	y = 538086x + 25514	0.9930	0.64	1.92	0.45	1.98	0.83	4.83	4.72
SCP	10– 1000	y = 616970x + 16708	0.9918	1.88	5.64	1.50	4.68	2.22	4.83	5.33
SMX	10 – 3000	y = 474730x - 1647.3	0.9979	2.89	8.67	2.06	4.49	1.83	4.74	4.37
SDM	100 – 3000	y = 483316x + 147304	0.9900	7.5	22.5	1.01	1.59	2.67	3.46	4.00

[a] Precision were investigated at the concentration of 500 $\mu g\ L^{-1}$

4.1.5 Analysis to real samples

The proposed micro-SPE method was applied to analysis of sulfonamides in five water samples collected from different sources in Maha Sarakham province Northeastern of Thailand. The samples were filtered through Whatman filter No. 1 and 0.45 μm membrane filter before extraction and analysis. The studied samples did not contain the sulfonamide residues. Matrix-match calibration was used in real sample analysis. The samples were spiked with the studied sulfonamides at different concentration in the range of 10-500 μg L^{-1}, before extraction and analysis. Wide linear range with R^2 of greater than 0.99 for all samples, were obtained.

The matrix effect (ME) was calculated by comparing the ratio of the matrix-matched curve that to solvent (according to Eq. (2)). Commonly, ME values between 80 and 120% relate to no matrix effects, ME values between 50 and 80% or 120 – 150% relate to minor MEs, and ME values lower than 50% or higher than 150% appertain to major MEs [86]. The results were presented in Table 9, MEs (%) are in the range of 89–118%, indicating that no ME to minor ME was found in the studied samples. The accuracy of the proposed method was evaluated in terms of %recovery. Extraction recoveries in the range of 81–119% were obtained with the RSDs of less than 14.3%. The overlaid chromatograms of blank and spiked samples are shown in Figure 18.

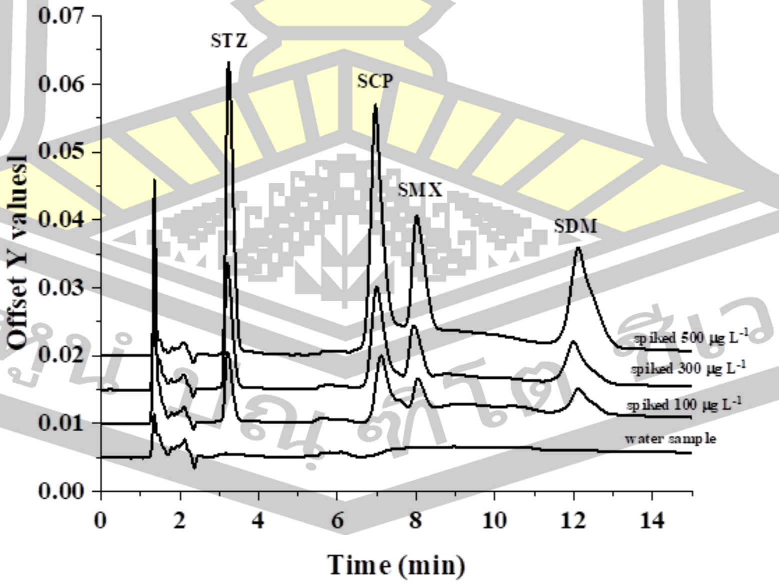


Figure 18 Chromatograms of water samples spiked with sulfonamide standard at 100, 300, and 500 μg L^{-1}.

Table 9 Matrix effect (%ME) of water samples.

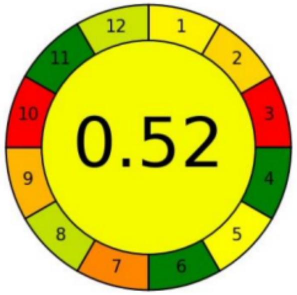
Sample	**STZ**	**SCP**	**SMX**	**SDM**
Water I	114.76	68.72	107.97	106.90
Water II	117.94	114.65	89.76	114.45
Water III	95.43	101.56	89.64	117.73
Water IV	113.29	114.51	107.71	113.43
Water V	113.76	105.33	114.96	108.11

4.1.6 Green characteristics of analytical procedures

Two greenness assessment tools, including Analytical Eco-Scale (AES) and AGREE methods were applied in this study to appraise the greenness. The Analytical Eco-Scale is that the ideal green analysis, which is calculated by deducting the sum of penalty points from 100 base points. Penalty points are assigned for each of the parameters of the analytical procedure that deviate from the ideal green analysis (reagent use, risk, energy and waste) [133]. The sum of the penalty points is then subtracted from 100 to obtain the numerical value of the AES. An excellent green standard is achieved by an AES value greater than 75, a satisfactory greenness by an AES value ranging from 50 to 75, and a deficient greenness by an AES value lower than 50. The analytical Eco-Score of 79 as shown in Table 10, confirms the greenness of the proposed and validated method as the excellent one.

AGREE is a recently introduced green metric system based on the conversion of method parameters correlated with regards to 12 basic principles of green analytical chemistry (GAC) [134]. The AGREE score of greater than 0.75 indicated an excellent greenness, the AGREE score of less than 0.75 but greater than 0.50 indicated the adequate greenness, and AGREE score of less than 0.50 indicated inadequate greenness [134]. Each part of the pictogram is depicted by AGREE clock-like graph with intuitive a green-yellow-red colour scale, which corresponds to the performance of each GAC principle. A result (as shown in Table 10) of 0.52 shows that the method or procedure is ecologically friendly and adheres to green analytical chemistry principles. The agreement observed between two different methods showed an excellent greenness characteristic of the current method proving the greenness of the whole procedures including all analytical steps for the studied method.

Table 10 Greenness assessment of the proposed method according to Analytical Eco-Scale.

Reagent	Amount PPs	Hazard PPs	Total PPs	AGREE Assessment
ACN (<10 mL)	2	4	4	 1. Sample treatment 2. Sample Amount 3. Device positioning 4. Sample prep. Stages 5. Automation, miniaturization 6. Derivatization 7. Waste 8. Analysis throughput 9. Energy consumption 10. Source of reagents 11. Toxicity 12. Operator's safety
MeOH (<10 mL)	1	6	6	
CTAB (<10 mL)	1	2	2	
TBABr (<10 mL)	1	1	1	
Dodecanoic acid (<10 mL)	1	2	2	
Instrument (HPLC-UV)			1	
Occupational hazard			0	
Waste (>10 mL)			5	
Sum of total PPs			21	
Analytical Eco-Scale score: 100 – 21 =		79 (Excellent green)		

4.1.7 Comparison with other sample preparation procedures

Some interesting parameters of the developed HDES2-MS as sorbent for micro-SPE with the previous procedures [12,4,135–139] were summarized in Table 11. The proposed method is superior to the others under greener and milder conditions, including using green features, shorter extraction/elution times, and lower temperatures. Because of the large specific surface area of MS and superhydrophobic behavior with selective adsorption of HDES2-MS, the investigated adsorbent was beneficial for the extraction of sulfonamide residues. The sensitivity of the proposed method in terms of limits of detection (LODs) is almost acceptable with fast adsorption times. Owing to the large specific surface area and selective adsorption of HDES2-MS, the developed adsorbent was useful for the extraction of sulfonamides. Some studies have used commercial sorbent that is easy to use but expensive. Furthermore, this developed method exhibited better reusability than commercial SPE sorbents, as most commercial sorbents cannot be reused after the extraction. Moreover, this method provided an improvement in the greenness of analytical methods by reducing the toxic organic solvent, and resources that were required for analytical procedure. Overall, the results of all greenness approaches indicated the excellent greener profile which the agreement observed between two different methods (Analytical Eco-Scale and AGREE pictograms). The proposed procedure provides a more efficient, rapid and simple extraction method for SAs determination in real samples.

Table 11 Comparison of analytical performance of the proposed method with other methods commonly used for SAs determination.

Pretreatment technique[a]	Sample	Instrument[b]	Linearity ($\mu g\ L^{-1}$)	LODs ($\mu g\ L^{-1}$ or $\mu g\ kg^{-1}$)	Desorption solvent	Ref.
ATP-SPE	Fish	HPLC-PDA	50-5000	6.4-12.9	1 mL of methanol	[135]
3D printed device coated Oasis MCX resin	Environmental water	HPLC-DAD	20-1000	0.6-6	3 mL of ammonium/methanol, 5:95, v/v	[136]
Dispersive micro SPE	Milk and honey	UHPLC-HRMS	0.005-20	0.003-1	1 mL of 5% NH_4OH in MeCN-H_2O, 50:50, v/v	[137]
MP-µ-SPE	Milk and chicken muscle	HPLC-UV	10-1000	0.38-0.62	0.1 mL of methanol- 1% acetic acid, 2:3, v: v	[138]
p-TFME	Environmental water	HPLC-DAD	0.5-500	0.14-0.52	200 µL of methanol	[4]
SPE	River, lake and waste water	HPLC-UV	5-3.0x10^4	1-10	5 mL of ammonia: methanol, 1:19 v/v	[139]
Silica/CTAB-SPE	environmental water and honey	HPLC-UV	9 –300	1 –3	500 µL of methanol	[12]
HDES2-MS	Environmental water	HPLC-UV	10-3000	3-30	500 µL of methanol	This work

[a] ATP-SPE = aqueous two phase with solid phase extraction, MP-µ-SPE = membrane-protected micro-solid phase extraction,
p-TFME = paper-based thin film microextraction, ionic liquid-based SD-LPME = ionic liquid based single-drop liquid-phase microextraction.

[b] HPLC = high performance liquid chromatography, UHPLC = ultra-high performance liquid chromatography, PDA = photodiode array, DAD = diode array detection, HRMS = high resolution mass spectrometry

4.2 Evaluation results of characterization, optimization and others of micro-SPE procedure using LDHs@Alg beads

4.2.1 Characterization of Mg-Al layered double hydroxide (Mg-Al LDHs) and Mg-Al@Alg beads

In order to establish the construction and structure of the studied Mg-Al LDHs and Mg-Al@Alg beads, several techniques were used including Fourier Transform Infrared Spectroscopy (FTIR), scanning electron microscopy (SEM) and thermogravimetric analysis (TGA).

The infrared spectra (FT-IR spectra) as can be seen in Figure 19. Alginate (a), the composite sample at Mg:Al LDH 1:1 mole ratio (b) and Mg-Al@Alg beads (c). For the Mg-Al LDH, the broad band around 3433 cm^{-1} cans be designated to the stretching vibrations of O–H of hydroxyl groups in the brucite-like layers and interlayer water molecules [140]. The band at 3000 cm^{-1} approximately is related to the hydrogen bond of H_2O to anions at the interlamellar space [141], while the band located around 1654 cm^{-1} was due to the H–O–H stretching and bending vibration of hydroxyl groups. The bands corresponding to the presence of NO_3^- as the interlayer anion, characterized by a trigonal planar symmetry inorganic nitrate has very characteristic spectra. There are three characteristic bands at around 1760, 1350 and 846 cm^{-1}. The N=O (1350 cm^{-1}) band is the strongest and is quite broad, while the other two absorptions are weaker and very narrow [142]. These vibrational bands are related to the various forms of NO_3^- anion interaction. Moreover, it was found that the bands between 400 and 800 cm^{-1} may be due to the superposition of magnesium and aluminum oxides' vibrational absorptions [142]. These results indicated that the Mg-Al LDH composite was synthesized successfully. Sodium alginate displays absorption band characteristics peak around 3200 cm^{-1}, which can be due to hydroxyl group (–OH), 1600 cm^{-1} asymmetric stretching vibration of COO^- groups (C=O bond), 1406 cm^{-1} (symmetric stretching vibration of COO^- groups), and 1029 cm^{-1} (elongation of C-O groups) [143]. For Mg-Al@Alg beads, it can be seen that the characteristic peaks show a similar pattern to alginate and Mg-Al LDH composites, showing the prominent peaks as follow: 3344, 1602, 1420, 1021 and 872 cm^{-1}. The above data demonstrate the successful combination of Mg-Al LDH with alginate to form Mg-Al@Alg beads for use as adsorbent in the present work.

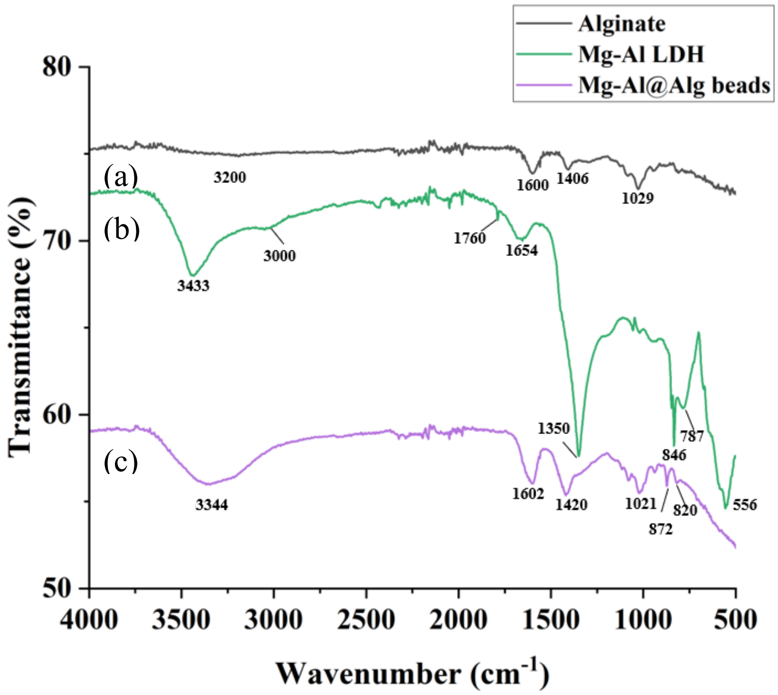


Figure 19 FI-IR spectrum of (a) alginate, (b) Mg-Al LDH and (c) Mg-Al@Alg beads.

Furthermore, SEM images indicated Mg-Al LDH is made up of aggregated irregular nanosheets, which is a typical hydrotalcite morphology. However, the high charge density of the LDHs layers and the high content of anionic species and molecule of water exhibits strong interlayer electrostatic interactions between the sheets, which persuade to a tight stacking of the lamellae, resulting in the agglomeration of LDH [144]. The result was shown in Figure 20(A). After combined of Mg-Al LDH and alginate for Mg-Al@Alg beads formation, it was found that, the LDH molecules are distributed evenly across the surface of the beads. The result was shown in Figure 20(B). When the Mg-Al@Alg beads was used as adsorbent for micro-SPE for sulfonamide analysis. After the target substance adsorption process, the surface of the adsorbent swells, indicating that the developed adsorbent has the ability to adsorb substances (as shown in Figure (20). After elution step, the analytes were removed from the surface of sorbent by desorption solvent, it can be seen that the surface of the adsorbent is only slightly degraded (as can be seen in Figure 20(D)) and remains in great condition. Resulting in the adsorbent provided excellent extraction potential and reusability.

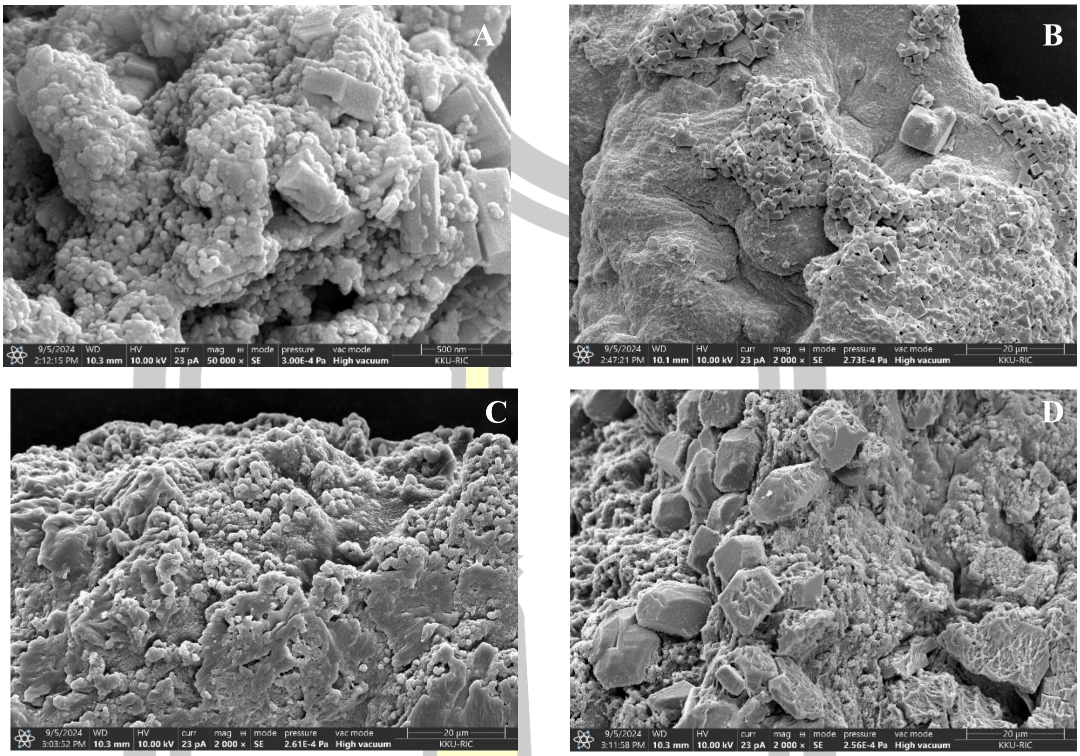


Figure 20 SEM image of (A) Mg-Al LDH, (B) Mg-Al LDH@Alg, (C) Mg-Al LDH@Alg adsorb and (D) Mg-Al LDH@Alg desorb.

4.2.2 Micro-SPE procedure using Mg-Al@Alg beads as adsorbent

In the process of optimization experiments, aqueous standard solutions containing 100 µg L^{-1} of each sulfonamide were investigated using the univariate method (which is the one-variable-at-a-time (OVAT) approach, where only one factor at a time is studied and optimized [4]. Various parameters were estimated consisting of LDHs component (Ni^{2+}:Al^{3+}, Mg^{2+}:Al^{3+} and Zn^{2+}:Al^{3+}) at molar ratio of 1:2, ratios of $Metal^{2+}$ (1 to 4), $Metal^{3+}$ (1 to 3), amount of sodium alginate(0.5, 1.0, 2.0 and 3.0 %w/v), amount of beads (0.01, 0.05, 0.10, 0.30 and 0.50 g), kind of surfactants (cetyltrimethylammonium bromide, sodium dodecyl sulfate and Triton X-114), concentrations of CTAB (0.20, 0.40, 0.60, 0.80 and 1.0 mmol L^{-1}), kind of desorption solvent (acetonitrile, methanol, ethanol, and water) and volume of desorption solvent (500, 750 and 1000 µL).

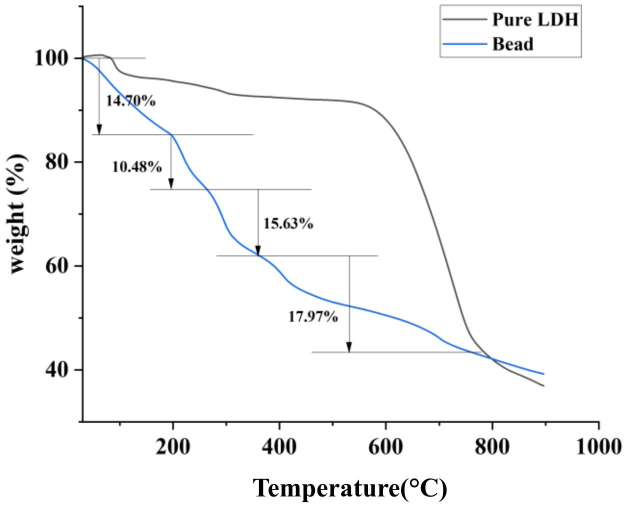


Figure 21 TGA curve of Mg-Al LDHs and Mg-Al@Alg beads.

The thermal properties of Mg-A@Alg (as can be seen in Figure 21) beads were analyzed using thermogravimetric analysis (TGA). The thermogram of Mg-Al@Alg beads provided the first mass loss 14.70% in the range of 90–190 °C approximately, refer to the water molecules at the structure of sorbent with weakly adsorbed were dehydrate. The second mass loss 10.48% appeared around 190-250 °C approximately, indicates the depolymerization of pyranose ring structure of alginate polymer. The third mass loss 15.63% between 250-380 °C approximately, provided connected with the ZnFe-LDHs dehydration and may corresponded the Mg-Al LDHs arrangements. Then another mass loss 17.97% was found at 700 °C approximately connected to the dehydorxylation [145,146]. In addition, the last mass loss between Mg-Al LDH material and Mg-Al@Alg beads has the same end which shows that they have the same composition of substances. These results indicated that the synthesized beads were mixed with alginate and LDH successfully.

4.2.3 Preparation of LDHs@Alg beads

4.2.3.1 LDHs synthesis

In this work, LDH as one of precursors for beads formation. The metals used in LDHs synthesis can be varied through the combination of different metal precursors used and the different ratio of M^{2+} to M^{3+} species in the metal layers were studied. Due to metals present in the LDH have been affect textual merits of the materials which could be impacting sorption capacity, including a change in interlayer free space and pore characteristics [147] to encourage comprehend the role the metals used in the LDH are having on sorption properties. Therefore, the LDH synthesis process should be varied. In present work three types of LDH were varied namely, Zn-Al LDH, Mg-Al LDH and Ni-Al. The result shown the Mg-Al LDH provides higher extraction efficiency than other LDH types (As can be seen in Figure 22). Therefore, the Mg-Al LDH was chosen as the optimum type of LDH. Meanwhile, the ratios of Mg^{2+} and Al^{3+} were studied were studied in the range 1 to 4 mole ratios in 100 mL DI water. The effect of Mg^{2+} (As can be seen at Figure 23) shown the extraction efficiency increased from 1:2 to 2:2 of Mg^{2+}: Al^{3+} ratios. When the proportion of Mg^{2+} was further increased, the extraction efficiency was found to decrease slightly. In the same way, the ratio of Mg^{2+}: Al^{3+} at 2:2 shown the highest extraction efficiency (the results shown in Figure 24). It may be caused by the smaller LDH ratios resulted in higher sorption capacities due to the percentage decrease in Al^{3+}, allowing for greater ease in anion exchange through improved anion mobility [147]. Therefore, the M^{2+}:M^{3+} proportion at 2:2 was selected for optimum condition for LDH synthesis.

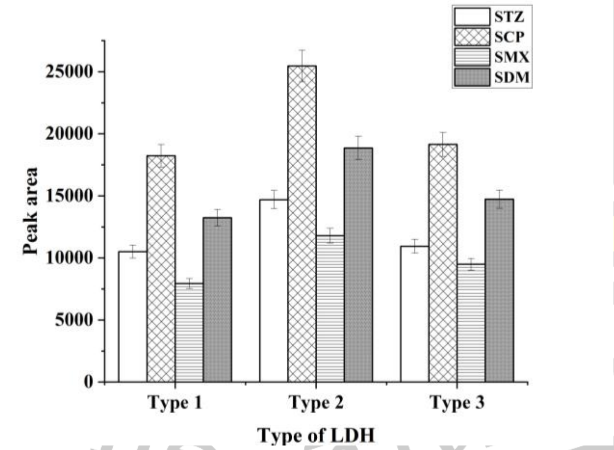


Figure 22 Type of LDH materials (n=3).

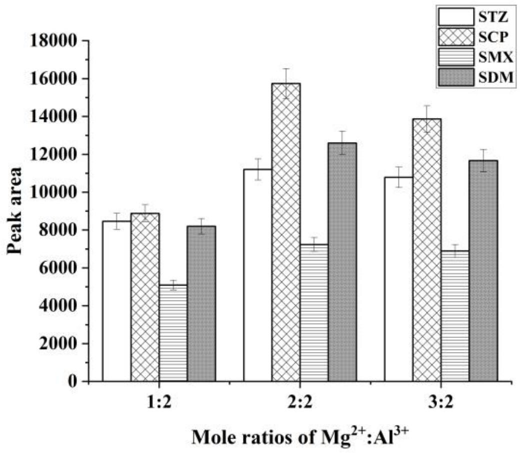


Figure 23 Effect of Mg^{2+} proportion (n=3).

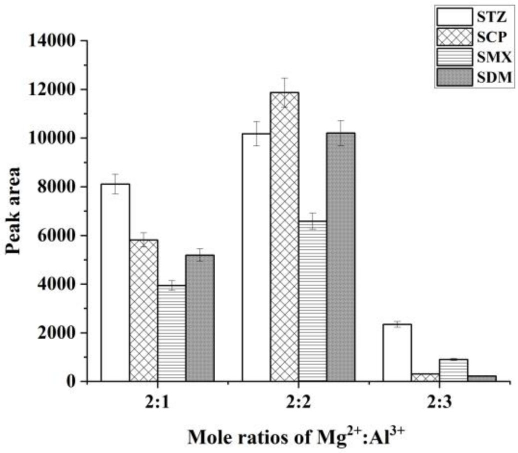


Figure 24 Effect of Al^{3+} proportion (n=3).

4.2.3.2 Effect of beads formation

In this work, the LDH beads was used as adsorbent for efficient micro-SPE for sulfonamides preconcentration. The proportion of LDH composite and alginate is the most important condition for beads formation. In the present work, the percent of alginate was studied. The percent of alginate was carried in the range of 0.5% to 4% with 1% of Mg-Al LDH composite. As a result of the amount of LDH greater than 1% will cause the proportion of LDH in the beads to be too high, causing the beads to be denatured and causing the beads to break. Moreover, the percent of sodium alginate was studied from 0.5 to 3%. Wherewith, the lower concentration of 0.5 % sodium alginate led to the shape of beads diameter smaller than 1 mm was obtained. In the other hand, the beads were difficult to produce, and with a solution of 3% sodium alginate was not able to break up the polymer solution jet into droplets [148]. Figure 25 shown that the 0.5% of sodium alginate provide the highest extraction efficiency toward the percent of sodium alginate toward the amount of alginate affects the shape of the dried beads, with higher alginate proportion resulting in a more rounded shape than beads with lower alginate content, resulting in a larger surface area exposed to the analytes than beads with higher alginate proportion. Consequently, the 0.5% sodium alginate was selected to Mg-Al@Alg beads formation.

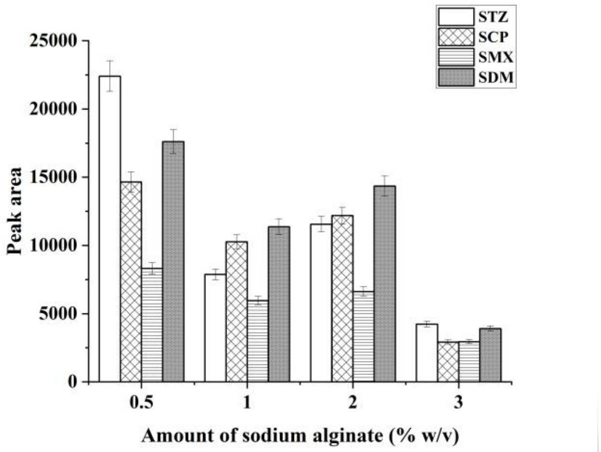


Figure 25 Effect of amount of sodium alginate (%w/v) (n=3).

4.2.4 Optimization of micro-SPE procedure

4.2.4.1 Type of sorbent

In this work, the effect of the performance enhancement of composite materials used as adsorbents, namely pure alginate, pure Mg-Al LDH, and a mixture of LDH and alginate, was studied as can be seen in Figure 26. The results show that both alginate and LDH have the ability to increase the concentration of the target substance. However, even though LDH has the preconcentration ability of the target analytes, its powder form makes it difficult to extract and collect the extraction phase. Since the powder particles of this synthesized nanomaterial are very small, during the extraction process, they may escape and leak out of the extraction system, resulting in decreased extraction efficiency. While alginate has the preconcentration performance of the target analytes, it still has a poor extraction efficiency. When alginate and LDH were mixed together in the form of beads, it was found that the extraction efficiency was much better when compared to the two pure substances. Therefore, it can be concluded that it is appropriate to develop LDH and alginate as a combined adsorbent in this work.

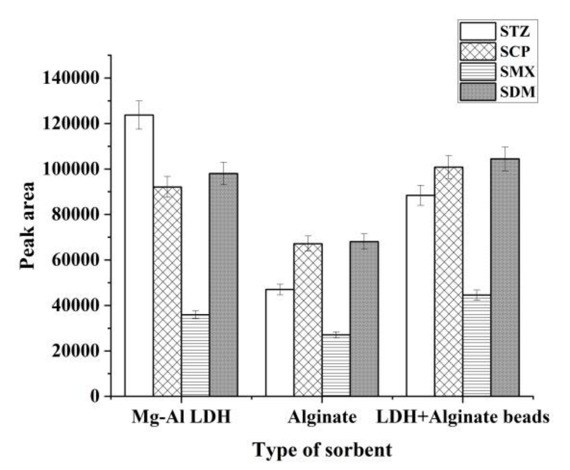


Figure 26 Type of sorbent (n=3)

4.2.4.2 Amount of prepared Mg-Al@Alg beads

The amount of prepared sorbent was varied in the proposed method for the high extraction efficiency were obtained. The prepared sorbent was studied in the range 0.01 to 0.5 g. The results (as shown in Figure 27) presented show that the extraction efficiency increased when the amount of sorbent increased from 0.01 to 0.05 g while the weight of sorbent was greater than 0.05 g, resulting in the extraction efficiency gradually decreasing. Therefore, the 0.05 g Mg-Al@Alg beads was selected as the optimum weight of sorbent in current method.

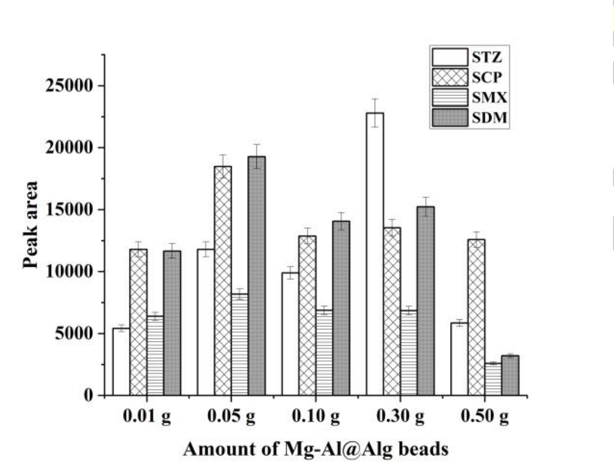


Figure 27 Effect of amount of Mg-Al@Alg beads (n=3).

4.2.4.3 Effect of kind of surfactant

Normally, the surfactant molecules containing two parts of them are hydrophobic and hydrophilic part. To increase the extraction efficiency, the surfactant is one of important role. Wherewith, the surfactant has the ability to increase the mass transfer potential of the analytes from the aqueous phase to the organic phase. Since, the surfactant addition was varied in this work. In the present work was studied with three various kinds of surfactant with different charge consisting of cationic surfactant, anionic surfactant and non-ionic surfactant represented in term of CTAB, SDS and Triton X-114, respectively. The result provided that the peak area of all sulfonamides extremely increased by two other surfactants., When the CTAB was added, all of the hydrophilic and hydrophobic parts of surfactant interacted with the analytes in aqueous. Then help to bring the analytes to interact at the surface of the adsorbent with CTAB as a mediator. The possible interaction of adsorption it may be occurred by various parts of adsorbent (as presented in Figure 30). The main adsorption interaction occurred by improves the adsorptive properties of the synthesized sorbent due to the CTAB as cationic surfactant was added to increase anionic retention, hydrophobicity [124,125]. Results in an increased adsorption mechanism on the LDH, where the target analytes can be directly adsorbed via hydrogen bonds with amine groups on SAs structure and hydroxyl groups on LDH and can also undergo adsorption via CTAB-mediated interactions via electrostatic and hydrophobic interactions. In addition, this surfactant also interacted with the surface of alginate. Resulting in the extraction efficiency increased. Therefore, the CTAB addition was selected in this work. The results are presented Figure 28.

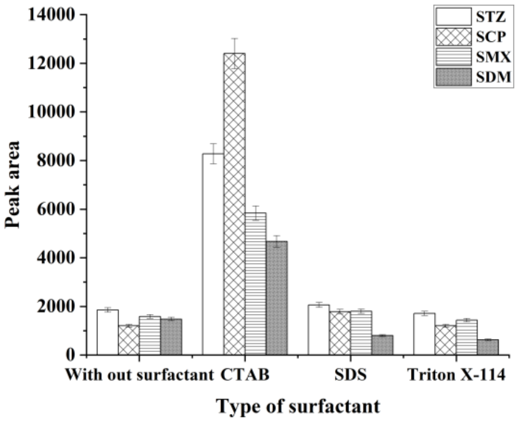


Figure 28 Type of surfactant (n=3).

4.2.4.4 Effect of selected surfactant concentration

Different selected concentrations were investigated in the range of 2 to 10 mM. The results are presented in Figure 29. The peak area of four sulfonamides gradually increased from 2 to 6 mM When the CTAB concentration up to 6 mM, then the peak area slightly decreased. Due to concentration of surfactant increased resulting in the viscosity increase, as a result the decreased analytes detection [11]. Thus, CTAB 6 mM was added in the current method.

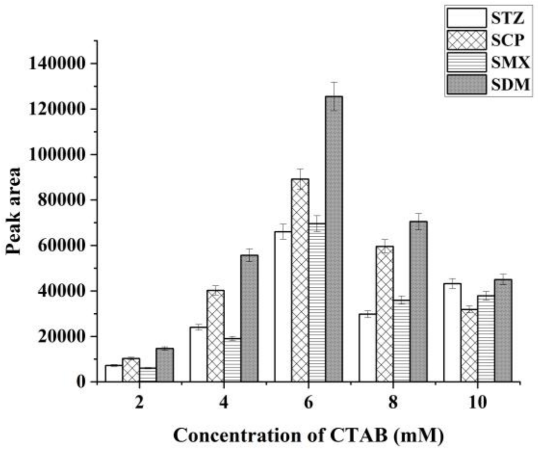


Figure 29 Effect of selected surfactant concentration (n=3).

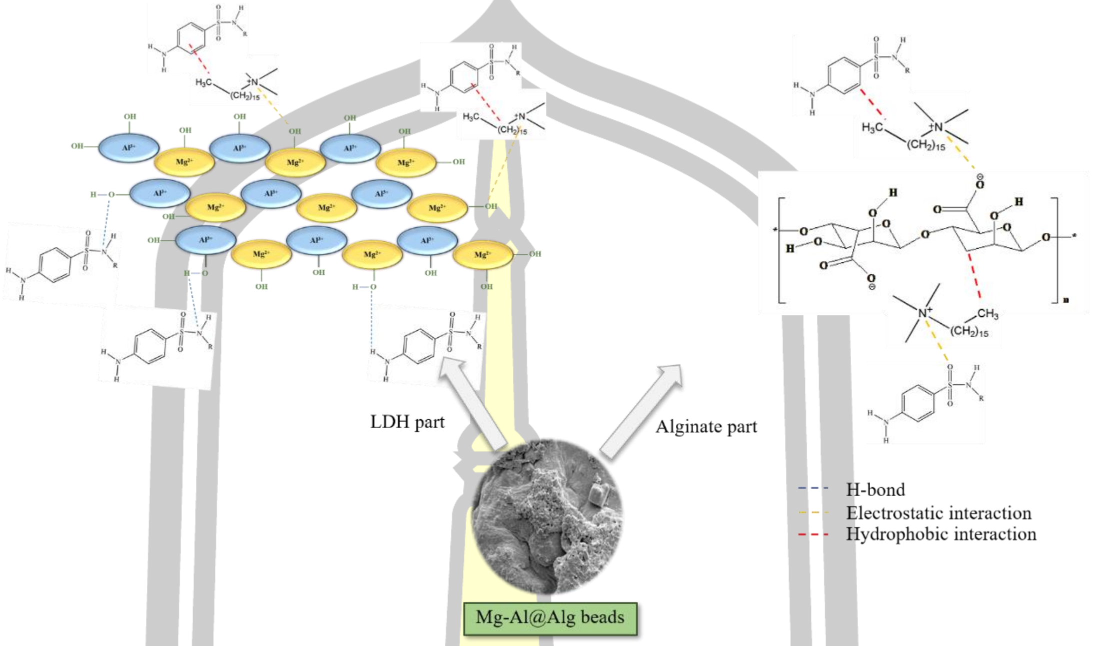


Figure 30 Scheme of possibility of beads adsorption mechanism.

4.2.4.5 Effect of type of desorption solvent

In this work, four desorption solvents were investigated, including DI water, acetonitrile, methanol and ethanol. As the results in Figure 31, acetonitrile, methanol and ethanol had ability for desorbing the target analytes. However, acetonitrile provides the best desorption power for studied STZ, SMX and SDM while ethanol provides the best desorption power for studied SCP but revealed lower desorption power of other analytes than acetonitrile. Therefore, acetonitrile was chosen as desorption solvent in the present method.

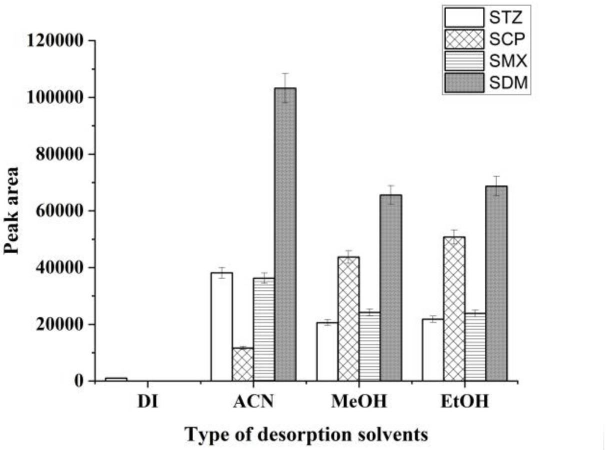


Figure 31 Effect of type of desorption solvent (n=3).

4.2.4.6 Effect of selected desorption solvent volume

The effect of selected desorption solvent volume was examined in the range of 500 to 1000 µL, due to the volume is less than 500 µl, it will result in the volume of the eluate phase being too small to be injected under UPLC conditions. The results shown that the extraction efficiency gradually decreased with desorption solvent volume increased. Owing to the use of desorption solvent consumption would reach to increase solubility of analytes resulting in the extraction efficiency decrease when the desorption solvent volume increases due to dilution effect. Hence, 500 µL acetonitrile was selected desorption solvent volume in this studied.

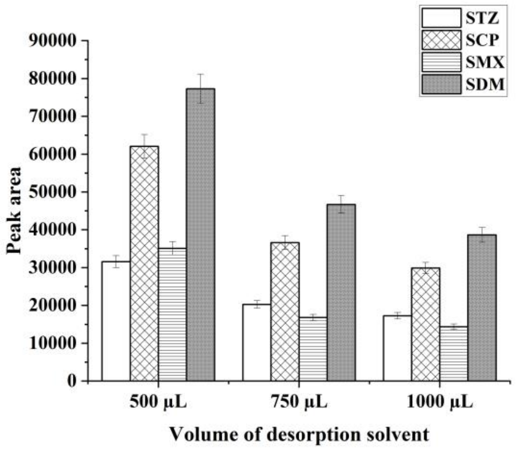


Figure 32 Effect of chosen desorption solvent volume (n=3).

4.2.4.7 Effect of pH

The pH of the solution is expected to play a significant role due to sulfonamides are amphoteric compounds whose molecular state is influenced by pH [151]. The effect of pH on the extraction efficiency by using the as-prepared sorbent was investigated with the aim of extracting sulfonamide antibiotics under their different forms including cationic, neutral or anionic. The highest extraction efficiency were obtained in the pH 6.6, in which SAs are in a neutral form (data not shown). Thus pH 6.6 was used for the studied experiments.

The optimal synthesis and extraction condition for the investigated method, were 1:1 molar ratio of Mg^{2+}: Al^{3+} for Mg-Al LDH synthesis, 1% of Mg-Al LDH and 0.5 % sodium alginate for Mg-Al@Alg beads formation, 0.05 g of Mg-Al@Alg beads. 0.2 M CTAB (150 µL), 500 µL of acetonitrile (as a desorption solvent) for micro-SPE. The optimum conditions are summarized in Table 12.

Table 12 The optimum conditions of micro-SPE for sulfonamide antibiotics analysis.

Parameters	**Optimum conditions**
LDH synthesis	1:1 molar ratio Mg^{2+}: Al^{3+}
Beads formation	1%Mg-Al LDH and 0.5 % SA
Amount of sorbent	0.05 g
Surfactant	0.2 M CTAB (150 µL)
Desorption solvent	500 µL acetonitrile

4.2.5 Reusability

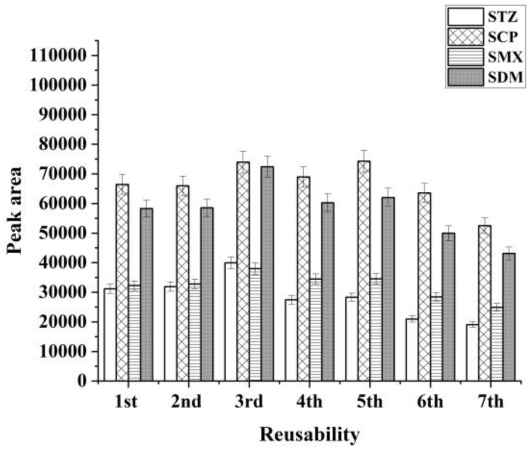


Figure 33 Reusability of Mg-Al@Alg beads for micro-SPE procedure.

The reusability of Mg-Al@Alg beads was studied. In the present work, acetonitrile was used as desorption solvent for desorbed sulfonamides from Mg-Al@Alg beads. After extraction process consist of adsorption and desorption step, the Mg-Al@Alg beads were washed by acetonitrile 5 mL for two times and dried before starting a new extraction cycle. The results provide that the efficiency of the Mg-Al@Alg beads relatively consistent in the first 5 extraction cycles, being reusable for up to five times. After that, the signal gradually decreased may be cause the loss of structural stability of the adsorbent.

4.2.6 Adsorption capacity

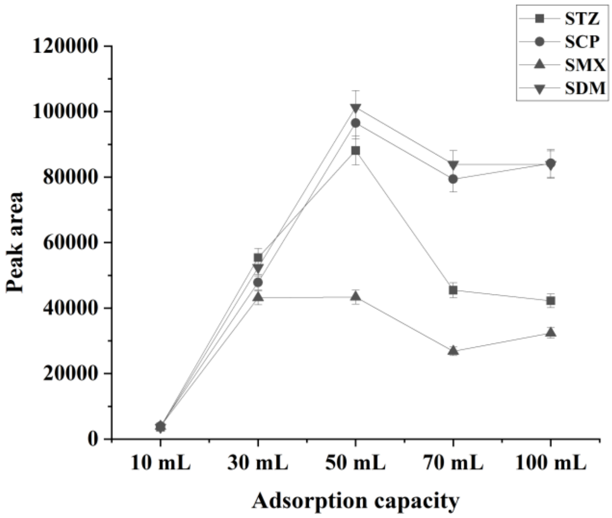


Figure 34 Adsorption capacity.

Briefly, adsorption capacity was studied using 0.1 mg L^{-1} sulfonamides with different volume from 10 to 100 mL were passed through 0.05 g of Mg-Al@Alg beads. The peak area gradually increased when the amount of analytes increased from 10 to 50 mL, the results represent the maximum volume at 50 mL, resulting in maximum adsorption capacity of Mg-Al@Alg beads at 100 mg kg^{-1} (calculated as follow eq. (4)). This work indicates an alternative adsorption sorbent namely Mg-Al@Alg beads, which exhibited excellent extraction performance using a small amount of adsorbent and excellent adsorption performance.

4.2.7 Analytical feature of developed method

The analytical figures of the developed method for the extraction of sulfonamides using as prepared material are summarized in Table 14. The linearity of the proposed method was evaluated by the analysis of working standard solutions of sulfonamides at nine different concentrations within the working range. Each concentration was injected three times. The method exhibited good linearities were achieved in the concentration range from 20 to 800 µg L^{-1} for sulfathiazole (STZ) and sulfachloropyridazine (SCP) and from 10 to 800 µg L^{-1} for sulfamethoxazole (SMX) and sulfadimethoxine (SDM) with R^2 more than 0.99. The LOQs and LODs were evaluated based on a signal-to-noise ratios and were based on analytical responses of 10 [124] and three times the background noise, respectively. LODs range from 3 to 6 μg L^{-1} and LOQs range from 9 to 18 μg L^{-1}. Good reproducibility (n = 5, %RSD ≤ 5.0) and precision (n = 3 × 5, %RSD < 5.0) were also obtained. The enrichment factors (EF) were calculated by comparing the slopes of the calibration graphs obtained by proposed method and direct UPLC. The analytical performances of sulfonamide determination by direct HPLC were shown in Table 13. The compared slope were found to be in the range of 19.52 to 43.40. The precision in term of intraday (n =5) and over several days (n = 5 × 3 days) were also investigated as the RSDs of retention time (t_R) and peak area of the studied compounds. High precisions were observed with RSD lower than 0.82 (t_R) and 7.47 (peak area), respectively. The chromatograms of the standard sulfonamides obtained from direct UPLC and micro-SPE-UPLC process are presented in Figure 35.

Table 13 Analytical performance of four sulfonamides by direct UPLC

Analyte	Linear range (μg L^{-1})	Linear equation	R^2	LOD (μg L^{-1})	LOQ (μg L^{-1})	Intra-day[a] precision (n=5), RSD (%)		Inter-day precision (n=3 × 5), RSD (%)	
						t_R	Peak area	t_R	Peak area
Sulfathiazole	90 – 3000	y = 19297x + 437.67	0.9987	10.0	30.0	0.47	2.77	0.61	2.38
Sulfamethazine	90 – 3000	y = 21174x - 924.58	0.9981	30.0	90.0	0.41	2.20	0.42	2.95
Sulfamethoxazole	90 – 3000	y = 21359x - 259.54	0.9979	30.0	90.0	1.64	1.98	1.33	1.81
Sulfadimethoxine	90 – 3000	y = 20426x + 241.33	0.9989	30.0	90.0	1.03	2.43	0.84	3.02

Precision were investigated at the concentration of 300 μg L^{-1}

Table 14 Analytical performance of the proposed method for determination of sulfonamides residues.

Analyte	Linear range (µg L^{-1})	Linear equation	R^2	LOD (µg L^{-1})	LOQ (µg L^{-1})	EF	Intra-day precision^a (n=5), RSD (%)				Inter-day precision (n=3 × 5), RSD (%)			
							t_R		Peak area		t_R		Peak area	
							50	**100**	**50**	**100**	**50**	**100**	**50**	**100**
STZ	20-800	y = 432850x + 4723.2	0.9918	6.0	18	22.43	0.65	0.48	4.93	5.16	0.55	0.53	5.68	7.47
SCP	20– 800	y = 919013x - 17147	0.9923	6.0	18	43.40	0.82	0.19	5.50	2.79	0.78	0.42	5.88	5.49
SMX	10 – 800	y = 416968x – 7347	0.9954	3.0	9.0	19.52	038	0.21	1.42	5.19	0.57	0.33	4.93	6.43
SDM	10 – 800	y = 634466x + 15387	0.9933	3.0	9.0	31.06	0.71	0.44	5.34	3.31	0.74	0.44	4.48	5.99

Precision were investigated at the concentration of 50 and 100 µg L^{-1}

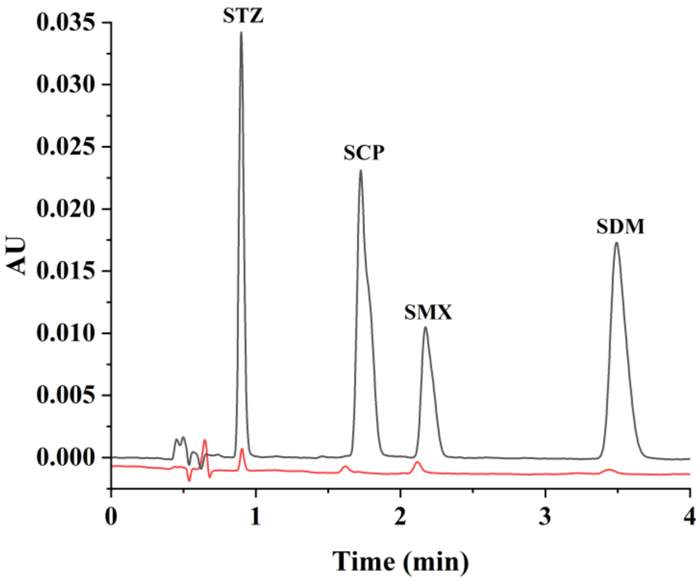


Figure 35 Chromatograms of the studied sulfonamides obtained by (red line) direct UPLC and (black line) the proposed micro-SPE method.

4.2.8 Analysis of real samples

The proposed micro-SPE method was applied to the analysis of sulfonamides in three honey samples. The honey samples were taken from local markets located in Maha Sarakham, Northeastern of Thailand. Each of samples were weighted about 5 g dissolved with DI water followed by diluted to 50 mL in volumetric flask. Then the solution was filtered through a Whatman filter No. 1. Then, 5 mL of filtrated solution was used for real sample extraction for sulfonamides analysis. The studied samples did not contain the sulfonamide residues. Matrix-match calibration was used in real sample analysis. The samples were spiked with the studied sulfonamides at different concentrations in the range of 20-800 μg L^{-1}, before extraction and analysis. Wide linear ranges with R^2 of greater than 0.99 for all samples, were obtained.

The matrix effect (ME) was calculated by comparing the ratio of the matrix-matched curve that to solvent (according to Eq. (2)). Generally, ME values between 80 and 120% relate to no matrix effects, ME values between 50 and 80% or 120 – 150% relate to minor MEs, and ME values lower than 50% or higher than 150% appertain to major MEs [125]. The results were presented in Table 15, from the results of ME% in the three honey samples, it was found that the matrix of most samples had a significant effect on the extraction. In samples I, II and III, the matrix effect values were in the range of 29.12 to 87.83%, indicating that no ME to major ME was found in the studied samples. The accuracy of the proposed method was evaluated in term of %recovery. Extraction recoveries in the range of 80.88–117.33% were obtained with the RSDs of less than 12.17%. The overlaid chromatograms of blank and spiked samples are shown in Figure 36 to 38.

Table 15 Matrix effects (%ME) of honey samples.

Analyte	**Matrix Effect (%)**		
	Honey I	**Honey II**	**Honey III**
STZ	40.06	33.70	54.25
SCP	53.61	46.16	62.09
SMX	87.83	43.20	61.98
SDM	65.07	53.28	29.12

Table 16 %Recovery of all honey samples

Analytes	**Spiked ($\mu g\ kg^{-1}$)**	**Recovery (%)**			
		STZ	**SCP**	**SMX**	**SDM**
Honey I	0	-	-	-	-
	50	111.12	112.68	80.88	83.98
	250	95.71	90.95	109.49	110.53
	500	100.93	102.08	97.84	97.58
Honey II	0	-	-	-	-
	50	114.21	87.98	91.39	87.11
	250	95.67	104.52	99.35	106.02
	500	100.95	98.64	100.21	98.63
Honey III	0	-	-	-	-
	50	108.22	97.06	117.33	113.46
	250	93.31	106.65	89.65	90.66
	500	101.55	98.69	104.85	102.15

Table 17 Marix matched calibration of honey samples

Analyte	Honey I		Honey II		Honey III	
	Matrix matched calibration	**R^2**	**Matrix matched calibration**	**R^2**	**Matrix matched calibration**	**R^2**
STZ	y=173390x – 1088	0.9989	y=145862x + 865.40	0.9987	y=234838x – 1207.80	0.9974
SCP	y=492709x – 5423.10	0.9953	y=424224x + 328.79	0.9987	y=570661x + 2467.60	0.9971
SMX	y=194872x + 194.52	0.9947	y=180155x + 333.52	0.9997	y=258452x – 2445.80	0.9938
SDM	y=412837x – 1041	0.9937	y=338025x + 1332.40	0.9979	y=184781x – 6518.60	0.9950

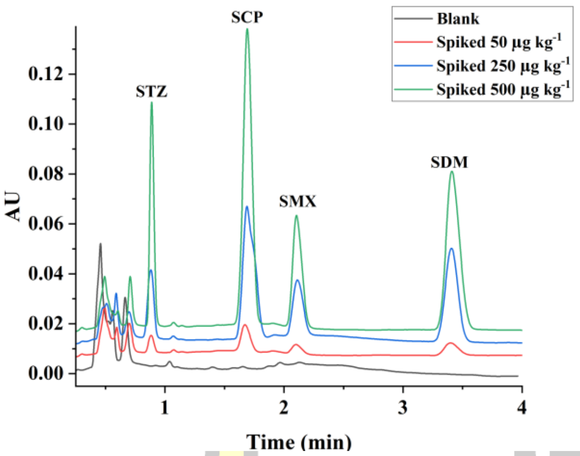


Figure 36 The overlaid chromatograms of blank and spiked honey sample I**.**

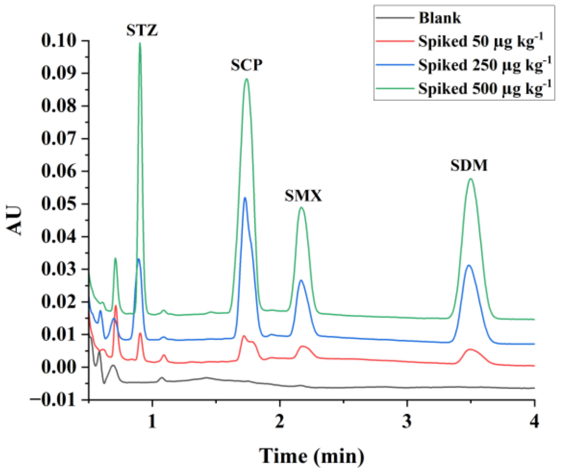


Figure 37 The overlaid chromatograms of blank and spiked honey sample II.

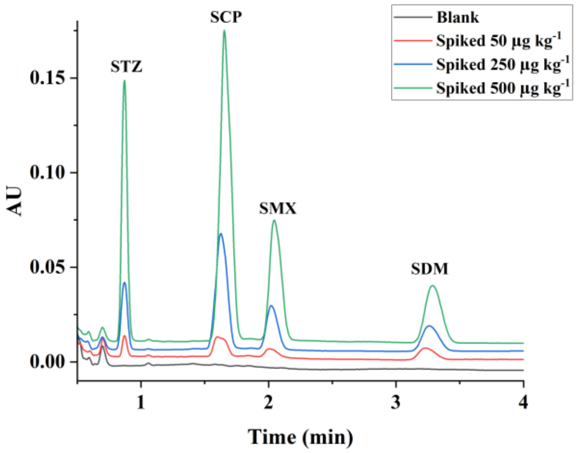


Figure 38 The overlaid chromatograms of blank and spiked honey sample III**.**

4.2.9 Green characteristic and analytical procedures

Two greenness assessment tools, including Analytical Eco-Scale (AES) and AGREE methods were applied in this study to appraise the greenness. The Analytical Eco-Scale is that the ideal green analysis, which is calculated by deducting the sum of penalty points from 100 base points. Penalty points are assigned for each of the parameters of the analytical procedure that deviate from the ideal green analysis (reagent use, risk, energy and waste) [133]. The sum of the penalty points is then subtracted from 100 to obtain the numerical value of the AES. An excellent green standard is achieved by an AES value greater than 75, a satisfactory greenness by an AES value ranging from 50 to 75, and a deficient greenness by an AES value lower than 50. The analytical Eco-Score of 71 as shown in Table 16, confirms the greenness of the proposed and validated method as the satisfactory one.

AGREE is a recently introduced green metric system based on the conversion of method parameters correlated with regards to 12 basic principles of green analytical chemistry (GAC) [134]. The AGREE score of greater than 0.75 indicated an excellent greenness, the AGREE score of less than 0.75 but greater than 0.50 indicated the adequate greenness, and AGREE score of less than 0.50 indicated inadequate greenness [134]. Each part of the pictogram is depicted by AGREE clock-like graph with intuitive a green-yellow-red colour scale, which corresponds to the performance of each GAC principle. A result (as shown in Table 18) of 0.54 shows that the method or procedure is ecologically friendly and adheres to green analytical chemistry principles. The agreement observed between two different methods indicated an excellent greenness characteristic of the current method proving the greenness of the whole procedures including all analytical steps for the studied method.

4.2.10 Comparison with other sample preparation procedures

Some interesting parameters of the developed alternative sorbent in term of Mg-Al@Alg beads for micro-SPE with the previous procedures [23,149-153] were summarized in Table 19. The proposed method is superior to the others under greener and milder conditions, including using green features, simple, fast, sorbent reusability, and lower temperatures. Because of the large specific surface area of Mg-Al LDH and alginate with selective adsorption of Mg-Al@Alg beads, the indicated adsorbent was beneficial for the extraction of sulfonamide residues. The sensitivity of the proposed method in terms of limit of detection (LOD) is almost acceptable with fast adsorption times. Owing to the large specific surface area and selective adsorption of Mg-Al@Alg beads, the developed adsorbent was useful for the extraction of sulfonamides. Some studies have used commercial sorbent that is easy to use but high cost. Moreover, this developed method exhibited better reusability than some reported sorbents, as most sorbents cannot be reused after the extraction. Moreover, this method provided an improvement in the greenness of analytical methods by reducing the toxic organic solvent, and resources that were required for analytical procedure. Overall, the results of all greenness approaches indicated the great greener profile which the agreement observed between two different methods (Analytical Eco-Scale and AGREE pictograms). The proposed procedure provides a more efficient, rapid and simple extraction method for the SAs determination in real samples.

Table 18 Greenness assessment of the proposed method according to Analytical Eco-Scale and AGREE assessment method.

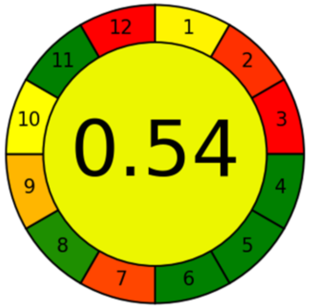
Reagent	Amount PPs	Hazard PPs	Total PPs	AGREE Assessment	
ACN (<10 mL)	2	4	4		
MeOH (<10 mL)	1	6	6		
CTAB (<10 mL)	1	2	2		
NaOH (<10 g)	1	1	1		
Na_2CO_3 (<10 g)	1	2	2		
$Mg(NO_3).6H_2O$ (<10 g)	1	2	2		
$Al(NO_3).9H_2O$ (<10 g)	1	4	4		
$CaCl_2$	1	1	1		
Technique (UPLC-PDA)			0	1. Sample treatment	7. Waste
Instrument (Hot plate)			2	2. Sample Amount	8. Analysis throughput
Occupational hazard			0	3. Device positioning	9. Energy consumption
Waste (>10 mL)			5	4. Sample prep. Stages	10. Source of reagents
Sum of total PPs			29	5. Automation, miniaturization	11. Toxicity
Analytical Eco-Scale score: 100 – 29 = 71 (Satisfactory green)				6. Derivatization	12. Operator’s safety

Table 19 Comparison of this proposed method with other procedures.

Technique	Sorbent	Sample	Linearity	LODs	Desorption solvent (mL)	Ref.
SPE-HPLC-MS	HP-COF(TpBD)	Pork, meat and chicken meat	0.5-200 $\mu g\ L^{-1}$	0.1-0.25	800 µL (acetone)	[23]
MSPE-HPLC	HCP/Fe_3O_4	Water and milk	2-400 ng mL^{-1}	0.21-2.5 ng mL^{-1}	2000 µL (ACN)	[151]
QuEChERS or SALLE or low temp cleanup-LC-QToF-MS	-	Baby food	5-120 µg kg^{-1}	2.5-10 µg kg^{-1}	100 µL (ACN: meOH 95:5 v/v, containing 0.1% formic acid)	[152]
MSPE-HPLC-DAD	silica-based magnetic	Milk	21-800 µg L^{-1}	7-14 µg L^{-1}	500 µL (1% formic acid/ 5 µg L^{-1} of IS)	[153]
PT-SPE-HPLC-UV	PANI- βHOXN-SO_4	Meat and honey	30-5x10^4 ng mL^{-1}	9.5-16.5 ng mL^{-1}	580 µL (meOH)	[154]
C18 cartridge column-HPLC-PDA	C18	Buffalo meat	31-2000 ng g^{-1}	31 ng g^{-1}	500 µL ACN/water (1:1)	[155]
Micro-SPE-UPLC-PDA	Mg-Al@Alg beads	Honey	20-500 µg L^{-1}	3-6 µg L^{-1}	500 µL (ACN)	This work

PT-SPE = pipette-tip solid phase extraction, HCP/Fe_3O_4 = magnetic hypercrosslinked polystyrene, HP-COF(TpBD) = hierarchical porous covalent organic frameworks (HP-COFs) foam and PANI- βHOXN-SO_4 = β-napthol –sulfate doped polyaniline nanofibers

CHAPTER V

CONCLUSIONS

This study presents alternative sorbents, namely hydrophobic deep eutectic solvent impregnated on melamine sponge (HDES2-MS) and Mg-Al layered double hydroxide combined with alginate beads (Mg-Al@Alg beads) for the efficient extraction and enrichment of sulfonamide residues using a simple micro-solid phase extraction (micro-SPE) prior to analysis by liquid chromatography (HPLC-UV and UPLC-PDA). For mechanism of HDES2-MS adsorption process, it was occurred by the hydrophobic interactions between hydrophobic tail of surfactant and hydrophobic sites of HDES2-MS while the hydrophilic parts of surfactant interacted with the sulfonamide in aqueous phase which allowed to improve sorption efficiency. While Mg-Al@Alg beads can be occurred by various parts conclude LDHs and alginate in sorbent structure through hydrogen bond, electrostatic interaction and hydrophobic interaction with CTAB as a medium between the analytes and the adsorbent.

Under optimum conditions, the developed method was applied to analysis four sulfonamide antibiotics namely STZ, SCP, SMX and SDM in water and honey samples. The results were not found sulfonamide antibiotics in all of samples. In addition, the developed method provided good extraction efficiency, LODs and LOQs lower than the maximum residue limit of sulfonamide antibiotics restricted by European Union, good repeatability with small amount of sorbent and organic solvent consumption were obtained.

This work found that the surfaces of the sponges were impregnated with hydrophobic deep eutectic solvents to exhibit a hydrophobic behavior with an aim to improve the adsorptive property and selectivity of the sponge, rendering it with a wide variety of practical applications. While Mg-Al@Alg beads achieves the goal of reusability and improves the extraction efficiency of the analytes successfully. Furthermore, green adsorbents are integrated with the principles of green analytical chemistry (GAC), which prioritizes reducing or eliminating harmful reagents and solvents. Therefore, the proposed methods have potential to be used as an alternative green extraction method for the determination of sulfonamide antibiotics residues from complex samples with good recoveries were obtained.

REFFERENCES

[1] K. Cherkashina, M. Voznesenskiy, O. Osmolovskaya, C. Vakh, and A. Bulatov, “Effect of surfactant coating of Fe3O4 nanoparticles on magnetic dispersive micro-solid phase extraction of tetracyclines from human serum,” *Talanta*, vol. 214, no. February, p. 120861, 2020, doi: 10.1016/j.talanta.2020.120861.

[2] K. Kümmerer, “Chemosphere Antibiotics in the aquatic environment – A review – Part I,” *Chemosphere*, vol. 75, no. 4, pp. 417–434, 2009, doi: 10.1016/j.chemosphere.2008.11.086.

[3] A. Almajed, M. Ahmad, A. R. A. Usman, and M. I. Al-Wabel, “Fabrication of sand-based novel adsorbents embedded with biochar or binding agents via calcite precipitation for sulfathiazole scavenging,” *J. Hazard. Mater.*, vol. 405, p. 124249, 2021, doi: 10.1016/j.jhazmat.2020.124249.

[4] M. S. Shahriman, S. Mohamad, N. N. Mohamad Zain, Y. Alias, K. Chandrasekaram, and M. Raoov, “Paper-based polymeric ionic liquid for thin film micro extraction of sulfonamides in environmental water samples prior to HPLC-DAD analysis,” *Microchem. J.*, vol. 171, no. July, p. 106798, 2021, doi: 10.1016/j.microc.2021.106798.

[5] B. Chen, W. Wang, and Y. Huang, “Talanta Cigarette filters as adsorbents of solid-phase extraction for determination of fluoroquinolone antibiotics in environmental water samples coupled with high-performance liquid chromatography,” *Talanta*, vol. 88, pp. 237–243, 2012, doi: 10.1016/j.talanta.2011.09.066.

[6] P. Shi and N. Ye, “Analytical Methods Magnetite – graphene oxide composites as a magnetic solid-phase extraction adsorbent for the determination of trace sulfonamides in water samples,” *Anal. Methods*, vol. 6, pp. 9725–9730, 2014, doi: 10.1039/C4AY02027H.

[7] L. Sun *et al.*, “Chemosphere Analysis of sulfonamides in environmental water

samples based on magnetic mixed hemimicelles solid-phase extraction coupled with HPLC – UV detection," *Chemosphere*, vol. 77, no. 10, pp. 1306–1312, 2009, doi: 10.1016/j.chemosphere.2009.09.049.

[8] I. Our, R. Carson, S. Spring, and O. Nielsen, "Drugs in the environment 1.," vol. 40, pp. 691–699, 2000.

[9] Q. Wang *et al.*, "Determination of four fl uoroquinolone antibiotics in tap water in Guangzhou and Macao," *Environ. Pollut.*, vol. 158, no. 7, pp. 2350–2358, 2010, doi: 10.1016/j.envpol.2010.03.019.

[10] E. Community, "amending Annexes I and III of Council Regulation (EEC) No 2377 / 90 laying Whereas dimetridazole , ronidazole , chloramphenicol ," no. 675, pp. 8–14, 1992.

[11] E. Karageorgou, N. Manousi, V. Samanidou, A. Kabir, and K. G. Furton, "Fabric phase sorptive extraction for the fast isolation of sulfonamides residues from raw milk followed by high performance liquid chromatography with ultraviolet detection," *FOOD Chem.*, vol. 196, pp. 428–436, 2016, doi: 10.1016/j.foodchem.2015.09.060.

[12] W. Khiaophong and J. Vichapong, "Green application of surfactant modified silica as effective sorbent for extraction and preconcentration of sulfonamide residues in environmental water and honey samples," *J. Chromatogr. A*, vol. 1718, p. 464720, 2024, doi: https://doi.org/10.1016/j.chroma.2024.464720.

[13] Y. Santaladchaiyakit and S. Srijaranai, "Analytical Methods A simplified ultrasound-assisted cloud-point extraction method coupled with high performance liquid chromatography for residue analysis of benzimidazole anthelmintics in water and milk samples," pp. 3864–3873, 2012, doi: 10.1039/c2ay25569c.

[14] L. Li, H. Zhang, M. Zhang, T. Wang, and X. Hou, "MIL-88B(Fe)/cellulose microspheres as sorbent for the fully automated dispersive pipette extraction towards trace sulfonamides in milk samples prior to UPLC-MS/MS analysis," *Anal. Chim. Acta*, vol. 1232, p. 340420, 2022, doi:

https://doi.org/10.1016/j.aca.2022.340420.

[15] M. K. Gupta *et al.*, "A comparative review on High-Performance Liquid Chromatography (HPLC), Ultra Performance Liquid Chromatography (UPLC) & High-Performance Thin Layer Chromatography (HPTLC) with current updates," *Curr. Issues Pharm. Med. Sci.*, vol. 35, no. 4, pp. 224–228, 2022, doi: 10.2478/cipms-2022-0039.

[16] L. Nováková, D. Solichová, and P. Solich, "Advantages of ultra performance liquid chromatography over high-performance liquid chromatography: Comparison of different analytical approaches during analysis of diclofenac gel," *J. Sep. Sci.*, vol. 29, no. 16, pp. 2433–2443, 2006, doi: 10.1002/jssc.200600147.

[17] M. Samadifar, Y. Yamini, M. M. Khataei, and M. Shirani, "Automated and semi-automated packed sorbent solid phase (micro) extraction methods for extraction of organic and inorganic pollutants," *J. Chromatogr. A*, vol. 1706, p. 464227, 2023, doi: https://doi.org/10.1016/j.chroma.2023.464227.

[18] W. I. T. Abd Halim *et al.*, "Performance analysis and green profile assessment of synthesised amino-functionalised magnetic silica nanocomposite for magnetic micro-solid phase extraction of penicillin antibiotics from milk samples," *J. Food Compos. Anal.*, vol. 127, p. 105944, 2024, doi: https://doi.org/10.1016/j.jfca.2023.105944.

[19] L. Aljerf, "A Novel Method to Chromatographically Resolution Of Sulphonamides By Vapour-Programmed Thin-Layer Chromatography," *MOJ Bioorganic Org. Chem.*, vol. 1, pp. 1–5, Sep. 2017, doi: 10.15406/mojboc.2017.01.00024.

[20] J. Ma, S. Fan, L. Sun, L. He, Y. Zhang, and Q. Li, "Jo ur l P re of," *Food Sci. Hum. Wellness*, 2020, doi: 10.1016/j.fshw.2020.05.002.

[21] Z. M. Saigl and F. M. Alshareef, "A Novel Solid Platform – Based Ag Nanoparticles Chemically Impregnated Activated Carbon for Selective Separation of Tungstate Species in Water : Kinetics and Thermodynamic

Study," vol. 1, pp. 1–13, 2020.

[22] K. G. Akpomie and J. Conradie, "Advances in application of cotton-based adsorbents for heavy metals trapping, surface modifications and future perspectives," *Ecotoxicol. Environ. Saf.*, vol. 201, no. May, p. 110825, 2020, doi: 10.1016/j.ecoenv.2020.110825.

[23] R. Shen, L. Huang, R. Liu, and Q. Shuai, "Determination of sulfonamides in meat by monolithic covalent organic frameworks based solid phase extraction coupled with high-performance liquid chromatography-mass spectrometric," *J. Chromatogr. A*, vol. 1655, p. 462518, 2021, doi: 10.1016/j.chroma.2021.462518.

[24] P. M. Frugeri *et al.*, "Magnetic restricted-access carbon nanotubes for the extraction/pre-concentration of organophosphates from food samples followed by spectrophotometric determination," *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.*, vol. 241, p. 118632, 2020, doi: https://doi.org/10.1016/j.saa.2020.118632.

[25] M. K. Abbasabadi and H. Shirkhanloo, *Speciation of cadmium in human blood samples based on Fe3O4-supported naphthalene-1-thiol- functionalized graphene oxide nanocomposite by ultrasound-assisted dispersive magnetic micro solid phase extraction*, vol. 189. Elsevier B.V., 2020. doi: 10.1016/j.jpba.2020.113455.

[26] T. Nema, E. C. Y. Chan, and P. C. Ho, "Talanta Application of silica-based monolith as solid phase extraction cartridge for extracting polar compounds from urine," vol. 82, pp. 488–494, 2010, doi: 10.1016/j.talanta.2010.04.063.

[27] Z. Lei, G. Zhang, Y. Ouyang, Y. Liang, Y. Deng, and C. Wang, "Simple fabrication of multi-functional melamine sponges," *Mater. Lett.*, vol. 190, pp. 119–122, 2017, doi: 10.1016/j.matlet.2016.12.082.

[28] E. K. Sam, J. Liu, and X. Lv, "Surface Engineering Materials of Superhydrophobic Sponges for Oil / Water Separation : A Review," 2021, doi: 10.1021/acs.iecr.0c05906.

[29] P. Makoś-Chełstowska and E. Słupek, “Superhydrophobic and superoleophilic melamine sponges impregnated with deep eutectic solvents for oil spill cleanup,” *Sep. Purif. Technol.*, vol. 324, p. 124537, 2023, doi: https://doi.org/10.1016/j.seppur.2023.124537.

[30] Y. Jiang *et al.*, “Talanta One-step fabrication of hydrophilic MIL-68 (Al)/ Chitosan-coated melamine sponge for vortex-assisted solid-phase extraction of parabens in water samples,” *Talanta*, vol. 68, no. September, p. 121799, 2020, doi: 10.1016/j.talanta.2020.121799.

[31] C. Wu *et al.*, “Natural Deep Eutectic Solvent-Catalyzed Selenocyanation of Activated Alkynes via an Intermolecular H-Bonding Activation Process,” *ACS Sustain. Chem. Eng.*, vol. 7, no. 2, pp. 2169–2175, Jan. 2019, doi: 10.1021/acssuschemeng.8b04877.

[32] T. Tan, M. Zhang, and Y. Wan, “Author ’ s Accepted Manuscript,” *Talanta*, 2015, doi: 10.1016/j.talanta.2015.11.041.

[33] M. O. and H. L. O. Laitinen, T. Suopajarvi, “Hydrophobic , superabsorbing aerogels from choline chloride-based deep eutectic solvent pretreated and silylated cellulose nanofibrils for selective oil removal,” 2017, doi: 10.1021/acsami.7b06304.

[34] J. Chen, W. Deng, X. Li, X. Wang, and Y. Xiao, “Hexafluoroisopropanol / Brij-35 based supramolecular solvent for liquid-phase microextraction of parabens in different matrix samples,” *J. Chromatogr. A*, vol. 1591, pp. 33–43, 2019, doi: 10.1016/j.chroma.2019.01.030.

[35] F. Shakirova, A. Shishov, and A. Bulatov, “Automated liquid-liquid microextraction and determination of sulfonamides in urine samples based on Schiff bases formation in natural deep eutectic solvent media,” *Talanta*, vol. 234, no. June, p. 122660, 2021, doi: 10.1016/j.talanta.2021.122660.

[36] K. Katthanet *et al.*, “Preconcentration of Heterocyclic Aromatic Amines in Edible Fried Insects Using Surfactant-Assisted Hydrophobic Deep Eutectic Solvent for Homogeneous Liquid–Liquid Microextraction prior to HPLC,”

ACS Omega, vol. 9, no. 3, pp. 3962–3970, Jan. 2024, doi: 10.1021/acsomega.3c08365.

[37] N. Gissawong, S. Mukdasai, S. Boonchiangma, S. Sansuk, and S. Srijaranai, "Chemosphere A rapid and simple method for the removal of dyes and organophosphorus pesticides from water and soil samples using deep eutectic solvent embedded sponge," *Chemosphere*, vol. 260, p. 127590, 2020, doi: 10.1016/j.chemosphere.2020.127590.

[38] M. Gilmore, É. N. McCourt, F. Connolly, P. Nockemann, M. Swadźba-Kwaśny, and J. D. Holbrey, "Hydrophobic Deep Eutectic Solvents Incorporating Trioctylphosphine Oxide: Advanced Liquid Extractants," *ACS Sustain. Chem. Eng.*, vol. 6, no. 12, pp. 17323–17332, Dec. 2018, doi: 10.1021/acssuschemeng.8b04843.

[39] C. Florindo, F. Lima, and I. M. Marrucho, "Hydrophobic Deep Eutectic Solvents: A Circular Approach to Purify Water Contaminated with Cipro fl oxacin," 2019, doi: 10.1021/acssuschemeng.9b02658.

[40] J. Cao and E. Su, "Hydrophobic deep eutectic solvents : the new generation of green solvents for diversified and colorful applications in green chemistry," *J. Clean. Prod.*, vol. 314, no. December 2020, p. 127965, 2021, doi: 10.1016/j.jclepro.2021.127965.

[41] P. Makoś, E. Słupek, and J. Gębicki, "Hydrophobic deep eutectic solvents in microextraction techniques – A review," *Microchem. J.*, vol. 152, no. October 2019, p. 104384, 2020, doi: 10.1016/j.microc.2019.104384.

[42] H. Abdolmohammad-Zadeh, Z. Rezvani, G. H. Sadeghi, and E. Zorufi, "Layered double hydroxides: A novel nano-sorbent for solid-phase extraction," *Anal. Chim. Acta*, vol. 685, no. 2, pp. 212–219, 2011, doi: 10.1016/j.aca.2010.11.035.

[43] W. Zhou, C. Wang, Y. Liu, W. Zhang, and Z. Chen, "Layered double hydroxides based ion exchange extraction for high sensitive analysis of non-steroidal anti-inflammatory drugs," *J. Chromatogr. A*, vol. 1515, pp. 23–29,

2017, doi: 10.1016/j.chroma.2017.07.047.

[44] Y. Wang, D. Zhang, M. Tang, S. Xu, and M. Li, “Electrocatalysis of gold nanoparticles/layered double hydroxides nanocomposites toward methanol electro-oxidation in alkaline medium,” *Electrochim. Acta*, vol. 55, no. 12, pp. 4045–4049, 2010, doi: 10.1016/j.electacta.2010.02.060.

[45] X. Zhang, Y. Wang, S. Dong, and M. Li, “Dual-site polydopamine spheres/CoFe layered double hydroxides for electrocatalytic oxygen reduction reaction,” *Electrochim. Acta*, vol. 170, pp. 248–255, 2015, doi: 10.1016/j.electacta.2015.04.170.

[46] C. Chen, P. Gunawan, and R. Xu, “Self-assembled Fe3O4-layered double hydroxide colloidal nanohybrids with excellent performance for treatment of organic dyes in water,” *J. Mater. Chem.*, vol. 21, no. 4, pp. 1218–1225, 2011, doi: 10.1039/c0jm01696a.

[47] S. Tang, Y. Chang, G. H. Chia, and H. K. Lee, *Selective extraction and release using (EDTA-Ni)-layered double hydroxide coupled with catalytic oxidation of 3,3’,5,5’-tetramethylbenzidine for sensitive detection of copper ion*, vol. 885. Elsevier B.V., 2015. doi: 10.1016/j.aca.2015.05.029.

[48] J. Kim *et al.*, “Magnetic nanocomposite spheres decorated with NiO nanoparticles for a magnetically recyclable protein separation system,” *Adv. Mater.*, vol. 22, no. 1, pp. 57–60, 2010, doi: 10.1002/adma.200901858.

[49] M. Ghadiri, W. Chrzanowski, and R. Rohanizadeh, “Biomedical applications of cationic clay minerals,” *RSC Adv.*, vol. 5, no. 37, pp. 29467–29481, 2015, doi: 10.1039/c4ra16945j.

[50] S. Bégu *et al.*, “New layered double hydroxides/phospholipid bilayer hybrid material with strong potential for sustained drug delivery system,” *Chem. Mater.*, vol. 21, no. 13, pp. 2679–2687, 2009, doi: 10.1021/cm803426j.

[51] S. Mallakpour, E. Azadi, and M. Dinari, “Removal of cationic and anionic dyes using Ca-alginate and Zn-Al layered double hydroxide/metal-organic framework,” *Carbohydr. Polym.*, vol. 301, p. 120362, 2023, doi:

https://doi.org/10.1016/j.carbpol.2022.120362.

[52] D. Chaara, F. Bruna, M. A. Ulibarri, K. Draoui, C. Barriga, and I. Pavlovic, “Organo/layered double hydroxide nanohybrids used to remove non ionic pesticides,” *J. Hazard. Mater.*, vol. 196, no. June, pp. 350–359, 2011, doi: 10.1016/j.jhazmat.2011.09.034.

[53] Y. L. Liu, J. Bin Zhou, R. S. Zhao, and X. F. Chen, “Using Zn/Al layered double hydroxide as a novel solid-phase extraction adsorbent to extract polycyclic aromatic hydrocarbons at trace levels in water samples prior to the determination of gas chromatography-mass spectrometry,” *Anal. Bioanal. Chem.*, vol. 404, no. 5, pp. 1603–1610, 2012, doi: 10.1007/s00216-012-6219-9.

[54] T. S. Anirudhan, P. S. Suchithra, and L. Divya, “Adsorptive potential of 2-mercaptobenzimidazole-immobilized organophilic hydrotalcite for Mercury(II) ions from aqueous phase and its kinetic and equilibrium profiles,” *Water. Air. Soil Pollut.*, vol. 196, no. 1–4, pp. 127–139, 2009, doi: 10.1007/s11270-008-9762-4.

[55] I. Mohiuddin *et al.*, “Starch-Mg/Al layered double hydroxide composites as an efficient solid phase extraction sorbent for non-steroidal anti-inflammatory drugs as environmental pollutants,” *J. Hazard. Mater.*, vol. 401, no. May 2020, p. 123782, 2021, doi: 10.1016/j.jhazmat.2020.123782.

[56] G. Ciarleglio, F. Cinti, E. Toto, and M. G. Santonicola, “Synthesis and Characterization of Alginate Gel Beads with Embedded Zeolite Structures as Carriers of Hydrophobic Curcumin,” *Gels*, vol. 9, no. 9, 2023, doi: 10.3390/gels9090714.

[57] R. Long *et al.*, “The easy-recoverable 3D Ni/Fe-LDH-SA gel ball encapsulated by sodium alginate is used to remove Ni2+ and Cu2+ in water samples,” *Colloids Surfaces A Physicochem. Eng. Asp.*, vol. 634, p. 127942, 2022, doi: https://doi.org/10.1016/j.colsurfa.2021.127942.

[58] I. Aswin Kumar and N. Viswanathan, “Development and Reuse of Amine-Grafted Chitosan Hybrid Beads in the Retention of Nitrate and Phosphate,” *J.*

Chem. Eng. Data, vol. 63, no. 1, pp. 147–158, 2018, doi: 10.1021/acs.jced.7b00751.

[59] Y. Ma *et al.*, “Gelatin/alginate composite nanofiber membranes for effective and even adsorption of cationic dyes,” *Compos. Part B Eng.*, vol. 162, no. January, pp. 671–677, 2019, doi: 10.1016/j.compositesb.2019.01.048.

[60] W. BRIAN, “Sulfonamides,” vol. 2024. MSD Manual, MSD Manual Professional Edition, 2024. [Online]. Available: https://www.msdmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-medications/sulfonamides

[61] Y. Farah, M. Oussama, and H. Jehad, “Sulfonamides: Historical Discovery Development (Structure-Activity Relationship Notes),” *In-vitro In-vivo In-silico J.*, vol. 1, no. 1, pp. 1–15, Jan. 2018, doi: https://doi.org/.

[62] A. Ovung and J. Bhattacharyya, “Sulfonamide drugs: structure, antibacterial property, toxicity, and biophysical interactions.,” *Biophys. Rev.*, vol. 13, no. 2, pp. 259–272, Apr. 2021, doi: 10.1007/s12551-021-00795-9.

[63] S. Manivel, B. S Gangadharappa, N. Elangovan, R. Thomas, O. A. Abu Ali, and D. I. Saleh, “Schiff base (Z)-4-((furan-2-ylmethylene)amino) benzenesulfonamide: Synthesis, solvent interactions through hydrogen bond, structural and spectral properties, quantum chemical modeling and biological studies,” *J. Mol. Liq.*, vol. 350, p. 118531, 2022, doi: https://doi.org/10.1016/j.molliq.2022.118531.

[64] Ö. Güleç *et al.*, “Bioactivity, cytotoxicity, and molecular modeling studies of novel sulfonamides as dual inhibitors of carbonic anhydrases and acetylcholinesterase,” *J. Mol. Liq.*, vol. 410, p. 125558, 2024, doi: https://doi.org/10.1016/j.molliq.2024.125558.

[65] K. A. Elsayad, G. F. Elmasry, S. T. Mahmoud, and F. M. Awadallah, “Sulfonamides as anticancer agents: A brief review on sulfonamide derivatives as inhibitors of various proteins overexpressed in cancer,” *Bioorg. Chem.*, vol. 147, p. 107409, 2024, doi: https://doi.org/10.1016/j.bioorg.2024.107409.

[66] Y. Li, T. Yang, X. Lin, J. Huang, J. Zeng, and Q. Cai, “Heliyon Isolation , identification , and optimization of conditions for the degradation of four sulfonamide antibiotics and their metabolic pathways in Pseudomonas stutzeri strain DLY-21,” *Heliyon*, vol. 10, no. 7, p. e29123, 2024, doi: 10.1016/j.heliyon.2024.e29123.

[67] C. Mejías, J. Martín, J. L. Santos, I. Aparicio, and E. Alonso, “Implications of polystyrene and polyamide microplastics in the adsorption of sulfonamide antibiotics and their metabolites in water matrices,” *Aquat. Toxicol.*, vol. 271, no. April, p. 106934, 2024, doi: 10.1016/j.aquatox.2024.106934.

[68] C. Gonza, S. Scharf, O. Gans, and E. Martı, “Environmental monitoring study of selected veterinary antibiotics in animal manure and soils in Austria,” vol. 148, pp. 570–579, 2007, doi: 10.1016/j.envpol.2006.11.035.

[69] N. A. Chugh, S. Bali, and A. Koul, “Integration of botanicals in contemporary medicine: road blocks, checkpoints and go-ahead signals,” *Integr. Med. Res.*, vol. 7, no. 2, pp. 109–125, 2018, doi: 10.1016/j.imr.2018.03.005.

[70] M. Popova and V. Bankova, “Contemporary methods for the extraction and isolation of natural products.,” *BMC chemistry*, vol. 17, no. 1. Switzerland, p. 68, Jun. 2023. doi: 10.1186/s13065-023-00960-z.

[71] T. Welton, “Ionic liquids: a brief history,” *Biophys. Rev.*, vol. 10, no. 3, pp. 691–706, 2018, doi: 10.1007/s12551-018-0419-2.

[72] J. T. Gorke, F. Srienc, and R. J. Kazlauskas, “Hydrolase-catalyzed biotransformations in deep eutectic solvents,” *Chem. Commun.*, no. 10, pp. 1235–1237, 2008, doi: 10.1039/b716317g.

[73] P. Domínguez de María and F. Hollmann, “On the (Un)greenness of Biocatalysis: Some Challenging Figures and Some Promising Options.,” *Front. Microbiol.*, vol. 6, p. 1257, 2015, doi: 10.3389/fmicb.2015.01257.

[74] C. Florindo, L. Romero, I. Rintoul, L. C. Branco, and I. M. Marrucho, “From Phase Change Materials to Green Solvents: Hydrophobic Low Viscous Fatty Acid–Based Deep Eutectic Solvents,” *ACS Sustain. Chem. Eng.*, vol. 6, no. 3,

pp. 3888–3895, Mar. 2018, doi: 10.1021/acssuschemeng.7b04235.

[75] S. L. Yang and Z. Q. Duan, “Insight into enzymatic synthesis of phosphatidylserine in deep eutectic solvents,” *Catal. Commun.*, vol. 82, pp. 16–19, 2016, doi: 10.1016/j.catcom.2016.04.010.

[76] S. Arriaga and A. Aizpuru, *Innovative non-aqueous phases and partitioning bioreactor configurations*, 1st ed., vol. 54. Elsevier Inc., 2019. doi: 10.1016/bs.ache.2018.12.004.

[77] L. Liu and T. Zhu, “Emulsification liquid-liquid microextraction based on deep eutectic solvents: An extraction method for the determination of sulfonamides in water samples,” *Anal. Methods*, vol. 9, no. 32, pp. 4747–4753, 2017, doi: 10.1039/c7ay01332a.

[78] A. Pochivalov, K. Cherkashina, A. Shishov, and A. Bulatov, “Microextraction of sulfonamides from milk samples based on hydrophobic deep eutectic solvent formation by pH adjusting,” *J. Mol. Liq.*, vol. 339, p. 116827, 2021, doi: 10.1016/j.molliq.2021.116827.

[79] M. Díaz-Álvarez and A. Martín-Esteban, “Preparation and further evaluation of L-menthol-based natural deep eutectic solvents as supported liquid membrane for the hollow fiber liquid-phase microextraction of sulfonamides from environmental waters,” *Adv. Sample Prep.*, vol. 4, no. October, 2022, doi: 10.1016/j.sampre.2022.100047.

[80] A. Isabel García-Valcarcel and A. Martín-Esteban, “Ultrasound-assisted extraction of sulfonamides from soil samples using natural deep eutectic solvents and their determination by liquid chromatography tandem mass spectrometry,” *Microchem. J.*, vol. 203, no. April, p. 110850, 2024, doi: 10.1016/j.microc.2024.110850.

[81] A. Alizadeh Irani, A. Dabbagh Moghaddam, S. Hadi, and V. Hadi, “Evaluation of some sulfonamide antibiotics residues in chicken meat samples using in-syringe counter current homogenous liquid–liquid extraction and magnetic deep eutectic solvent-based dispersive liquid–liquid microextraction and

HPLC–DAD," *Microchem. J.*, vol. 201, p. 110518, 2024, doi: https://doi.org/10.1016/j.microc.2024.110518.

[82] R. Costa, "Newly Introduced Sample Preparation Techniques: Towards Miniaturization," *Crit. Rev. Anal. Chem.*, vol. 44, no. 4, pp. 299–310, 2014, doi: 10.1080/10408347.2013.860874.

[83] S. Li *et al.*, "Synthesis of nitrogen-rich magnetic hypercrosslinked polymer as robust adsorbent for the detection of neonicotinoids in honey, tomatoes, lettuce and Chinese cabbage," *J. Chromatogr. A*, vol. 1677, 2022, doi: 10.1016/j.chroma.2022.463326.

[84] E. Ragheb, M. Shamsipur, F. Jalali, M. Sadeghi, N. Babajani, and N. Mafakheri, "Magnetic solid-phase extraction using metal–organic framework-based biosorbent followed by ligandless deep-eutectic solvent-ultrasounds-assisted dispersive liquid–liquid microextraction (DES-USA-DLLME) for preconcentration of mercury (II)," *Microchem. J.*, vol. 166, no. February, 2021, doi: 10.1016/j.microc.2021.106209.

[85] M. Zhang *et al.*, "Miniaturized kapok fiber-supported liquid extraction for convenient extraction of pesticide residues in vegetable oils: Determination of organochlorine pesticides as a proof-of-concept study," *Talanta*, vol. 253, no. July 2022, p. 123982, 2023, doi: 10.1016/j.talanta.2022.123982.

[86] N. N. Naing, S. C. Tan, and H. K. Lee, *Micro-solid-phase extraction*. Elsevier Inc., 2019. doi: 10.1016/B978-0-12-816906-3.00016-9.

[87] F. Khoshoei-Darki and F. Momenbeik, "Melamine sponges incorporated azo-linked porous organic polymer as adsorbent for extraction and determination of six B vitamins using pipette tip micro solid-phase extraction," *J. Chromatogr. A*, vol. 1727, p. 464978, 2024, doi: https://doi.org/10.1016/j.chroma.2024.464978.

[88] M. T. García-Valverde, T. Chatzimitakos, R. Lucena, S. Cárdenas, and C. D. Stalikas, "Melamine Sponge Functionalized with Urea-Formaldehyde Co-Oligomers as a Sorbent for the Solid-Phase Extraction of Hydrophobic

Analytes,” *Molecules*, vol. 23, no. 10. 2018. doi: 10.3390/molecules23102595.

[89] Z. Lei, G. Zhang, Y. Deng, and C. Wang, “Surface modification of melamine sponges for pH-responsive oil absorption and desorption,” *Appl. Surf. Sci.*, vol. 416, pp. 798–804, 2017, doi: 10.1016/j.apsusc.2017.04.165.

[90] Y. Zeng *et al.*, “Excellent regeneration, easy separation and high capacity of 3D chitosan–melamine sponge composites for anionic dye removal,” *New J. Chem.*, vol. 47, no. 13, pp. 6342–6352, 2023, doi: 10.1039/D2NJ05954A.

[91] H. J. Kim, M. H. Jeong, H. J. Park, W. C. Kim, and J. E. Kim, “Development of an immunoaffinity chromatography and HPLC-UV method for determination of 16 sulfonamides in feed,” *Food Chem.*, vol. 196, pp. 1144–1149, 2016, doi: 10.1016/j.foodchem.2015.10.014.

[92] S. Dowlatshah, E. Santigosa, M. Saraji, and M. R. Payán, “A selective and efficient microfluidic method-based liquid phase microextraction for the determination of sulfonamides in urine samples,” *J. Chromatogr. A*, vol. 1652, p. 462344, 2021, doi: 10.1016/j.chroma.2021.462344.

[93] E. Patyra, M. Przeniosło-Siwczynska, and K. Kwiatek, “Determination of sulfonamides in feeds by high-performance liquid chromatography after fluorescamine precolumn derivatization,” *Molecules*, vol. 24, no. 3, 2019, doi: 10.3390/molecules24030452.

[94] Y. J. Ma *et al.*, “Dispersive solid-phase extraction and dispersive liquid–liquid microextraction for the determination of flavor enhancers in ready-to-eat seafood by HPLC-PDA,” *Food Chem.*, vol. 309, 2020, doi: 10.1016/j.foodchem.2019.125753.

[95] W. Sun, X. Hu, Y. Xiang, L. Zhang, and N. Ye, “Rapid fabrication of magnetic covalent organic frameworks for the effective extraction and determination of sulfonamides in shrimp samples,” *Talanta Open*, vol. 8, no. July, p. 100255, 2023, doi: 10.1016/j.talo.2023.100255.

[96] L. Ma, Y. Gu, L. Guo, and K. Wang, “The determination of 11 sulfonamide antibiotics in water and foods by developing a N-rich magnetic covalent

organic framework combined with ultra-high performance liquid chromatography-tandem mass spectrometry††Electronic supplementary information (ESI) a," *RSC Adv.*, vol. 14, no. 30, pp. 21318–21327, 2024, doi: https://doi.org/10.1039/d4ra02530j.

[97] X. C. Huang, H. Chen, S. L. Wei, and J. K. Ma, "A novel enrichment and sensitive method for rapid determination of 4 sulfonamide antibiotics residues in fish," *Lwt*, vol. 199, no. April, 2024, doi: 10.1016/j.lwt.2024.116148.

[98] M. Richetta, M. Pg, A. Mattoccia, A. Varone, and R. Pizzoferrato, "Journal of Material Sciences & Engineering Layered Double Hydroxides : Tailoring Interlamellar Nanospace for a Vast Field of Applications," vol. 6, no. 4, 2017, doi: 10.4172/2169-0022.1000360.

[99] K. Goh, T. Lim, and Z. Dong, "Application of layered double hydroxides for removal of oxyanions : A review," vol. 42, pp. 1343–1368, 2008, doi: 10.1016/j.watres.2007.10.043.

[100] S. Marappa and P. V. Kamath, "Structure of the Carbonate-Intercalated Layered Double Hydroxides : A Reappraisal," pp. 2–6, 2015, doi: 10.1021/acs.iecr.5b03207.

[101] C. Forano, U. Costantino, V. Prévot, and C. T. Gueho, "Layered double hydroxides (LDH)," *Dev. Clay Sci.*, vol. 5, no. September 2005, pp. 745–782, 2013, doi: 10.1016/B978-0-08-098258-8.00025-0.

[102] F. Cavani, F. Trifirò, and A. Vaccari, "Hydrotalcite-type anionic clays: Preparation, properties and applications.," *Catal. Today*, vol. 11, no. 2, pp. 173–301, 1991, doi: 10.1016/0920-5861(91)80068-K.

[103] A. Béres, I. Pálinkó, I. Kiricsi, J. B. Nagy, Y. Kiyozumi, and F. Mizukami, "Layered double hydroxides and their pillared derivatives - Materials for solid base catalysis; synthesis and characterization," *Appl. Catal. A Gen.*, vol. 182, no. 2, pp. 237–247, 1999, doi: 10.1016/S0926-860X(99)00009-5.

[104] L. Perioli, T. Posati, M. Nocchetti, F. Bellezza, U. Costantino, and A. Cipiciani, "Intercalation and release of antiinflammatory drug diclofenac into

nanosized ZnAl hydrotalcite-like compound," *Appl. Clay Sci.*, vol. 53, no. 3, pp. 374–378, 2011, doi: 10.1016/j.clay.2010.06.028.

[105] C. Manzi-Nshuti, P. Songtipya, E. Manias, M. del M. Jimenez-Gasco, J. M. Hossenlopp, and C. A. Wilkie, "Polymer nanocomposites using zinc aluminum and magnesium aluminum oleate layered double hydroxides: Effects of the polymeric compatibilizer and of composition on the thermal and fire properties of PP/LDH nanocomposites," *Polym. Degrad. Stab.*, vol. 94, no. 11, pp. 2042–2054, 2009, doi: 10.1016/j.polymdegradstab.2009.07.013.

[106] H. Ai *et al.*, "A novel glucose sensor based on monodispersed Ni/Al layered double hydroxide and chitosan," *Biosens. Bioelectron.*, vol. 24, no. 4, pp. 1048–1052, 2008, doi: 10.1016/j.bios.2008.07.039.

[107] D. Tonelli, E. Scavetta, and M. Giorgetti, "Layered-double-hydroxide-modified electrodes: Electroanalytical applications," *Anal. Bioanal. Chem.*, vol. 405, no. 2–3, pp. 603–614, 2013, doi: 10.1007/s00216-012-6586-2.

[108] L. V. Constantino *et al.*, "Sorption-desorption of selenite and selenate on Mg-Al layered double hydroxide in competition with nitrate, sulfate and phosphate," *Chemosphere*, vol. 181, pp. 627–634, 2017, doi: 10.1016/j.chemosphere.2017.04.071.

[109] A. Violante, M. Pucci, V. Cozzolino, J. Zhu, and M. Pigna, "Sorption/desorption of arsenate on/from Mg-Al layered double hydroxides: Influence of phosphate," *J. Colloid Interface Sci.*, vol. 333, no. 1, pp. 63–70, 2009, doi: 10.1016/j.jcis.2009.01.004.

[110] B. M. V. da Gama, R. Selvasembian, D. A. Giannakoudakis, K. S. Triantafyllidis, G. McKay, and L. Meili, "Layered Double Hydroxides as Rising-Star Adsorbents for Water Purification: A Brief Discussion," *Molecules*, vol. 27, no. 15, 2022, doi: 10.3390/molecules27154900.

[111] A. L. Johnston, E. Lester, O. Williams, and R. L. Gomes, "Impacts of multi-pollutants on sulfonamide antibiotic removal from water matrices using layered double hydroxide sorbents," *Environ. Technol. Innov.*, vol. 33, no. November

2023, p. 103490, 2024, doi: 10.1016/j.eti.2023.103490.

[112] M. Li, A. Dopilka, A. N. Kraetz, H. Jing, and C. K. Chan, “Layered Double Hydroxide/Chitosan Nanocomposite Beads as Sorbents for Selenium Oxoanions,” *Ind. Eng. Chem. Res.*, vol. 57, no. 14, pp. 4978–4987, 2018, doi: 10.1021/acs.iecr.8b00466.

[113] J. Wang *et al.*, “A hybrid monolithic column based on layered double hydroxide-alginate hydrogel for selective solid phase extraction of lead ions in food and water samples,” *Food Chem.*, vol. 257, no. August 2017, pp. 155–162, 2018, doi: 10.1016/j.foodchem.2018.02.143.

[114] L. Meili *et al.*, “MgAl-LDH/Biochar composites for methylene blue removal by adsorption,” *Appl. Clay Sci.*, vol. 168, no. October 2018, pp. 11–20, 2019, doi: 10.1016/j.clay.2018.10.012.

[115] Y. T. Lai *et al.*, “Green Treatment of Phosphate from Wastewater Using a Porous Bio-Templated Graphene Oxide/MgMn-Layered Double Hydroxide Composite,” *iScience*, vol. 23, no. 5, p. 101065, 2020, doi: 10.1016/j.isci.2020.101065.

[116] P. Karthikeyan and S. Meenakshi, “Development of sodium alginate@ZnFe-LDHs functionalized beads: Adsorption properties and mechanistic behaviour of phosphate and nitrate ions from the aqueous environment,” *Environ. Chem. Ecotoxicol.*, vol. 3, pp. 42–50, 2021, doi: 10.1016/j.enceco.2020.11.003.

[117] A. S. Yazdi, “Surfactant-based extraction methods,” *Trends Anal. Chem.*, vol. 30, no. 6, pp. 918–929, 2011, doi: 10.1016/j.trac.2011.02.010.

[118] P. Arnnok, N. Patdhanagul, and R. Burakham, “Dispersive solid-phase extraction using polyaniline-modified zeolite NaY as a new sorbent for multiresidue analysis of pesticides in food and environmental samples,” *Talanta*, vol. 164, pp. 651–661, 2017, doi: 10.1016/j.talanta.2016.11.003.

[119] Y. Feng, Y. Wang, Y. Wang, X. Zhang, and J. Yao, “In-situ gelation of sodium alginate supported on melamine sponge for efficient removal of copper ions,” *J. Colloid Interface Sci.*, 2017, doi: 10.1016/j.jcis.2017.10.036.

[120] Z. Gao *et al.*, “Functionalized melamine sponge based on β-cyclodextrin-graphene oxide as solid-phase extraction material for rapidly pre-enrichment of malachite green in seafood,” *Microchem. J.*, vol. 150, no. August, p. 104167, 2019, doi: 10.1016/j.microc.2019.104167.

[121] P. K. Naik, S. Paul, and T. Banerjee, “Physiochemical Properties and Molecular Dynamics Simulations of Phosphonium and Ammonium Based Deep,” *J. Solution Chem.*, no. 0123456789, 2019, doi: 10.1007/s10953-019-00903-0.

[122] R. Chromá, V. Andruch, and P. Makos, “Closer look into the structures of tetrabutylammonium bromide – glycerol-based deep eutectic solvents and their mixtures with water,” vol. 338, pp. 1–11, 2021, doi: 10.1016/j.molliq.2021.116676.

[123] R. Chromá, M. Vilková, I. Shepa, P. Mako, and V. Andruch, “Investigation of tetrabutylammonium bromide-glycerol-based deep eutectic solvents and their mixtures with water by spectroscopic techniques,” vol. 330, pp. 13–16, 2021, doi: 10.1016/j.molliq.2021.115617.

[124] N. Altunay, A. Elik, and R. Gürkan, “Preparation and application of alcohol based deep eutectic solvents for extraction of curcumin in food samples prior to its spectrophotometric determination,” *Food Chem.*, p. 125933, 2019, doi: 10.1016/j.foodchem.2019.125933.

[125] J. Serna-Vázquez, M. Z. Ahmad, G. Boczkaj, and R. Castro-Muñoz, “Latest Insights on Novel Deep Eutectic Solvents (DES) for Sustainable Extraction of Phenolic Compounds from Natural Sources.,” *Molecules*, vol. 26, no. 16, Aug. 2021, doi: 10.3390/molecules26165037.

[126] Q. Zheng, F. Yang, Q. Sun, H. Tan, and X. Wang, “The eutectic and physicochemical properties of the carboxylic-acid-based deep eutectic solvents,” *J. Mol. Liq.*, vol. 410, p. 125639, 2024, doi: https://doi.org/10.1016/j.molliq.2024.125639.

[127] R. Mirzajani and J. B. Kha, “Electrospun nanofiber composite based on

bimetallic metal–organic framework/halloysite nanotubes/deep eutectic solvents/molecularly imprinted polymers for thin film microextraction of sulfonamides in milk, eggs and chicken meat by HPLC analysis," *Microchem. J.*, vol. 203, p. 110950, 2024, doi: https://doi.org/10.1016/j.microc.2024.110950.

[128] P. Rattanaphonsaen *et al.*, "A facile and green alternative method for preconcentration of triazole fungicides using fabrication of melamine sponge anchoring with Ni/Al-LDH adsorbent followed by HPLC analysis," *Microchem. J.*, vol. 203, p. 110928, 2024, doi: https://doi.org/10.1016/j.microc.2024.110928.

[129] "Surfactant-assisted dispersive liquid – liquid microextraction of nitrazepam and lorazepam from plasma and urine samples followed by high-performance liquid chromatography with UV analysis", doi: 10.1002/jssc.201500586.

[130] M. Larsen and M. Whitney, "Edwin m.," 1962.

[131] G. Yusakul, C. Thammakhet-Buranachai, S. Poorahong, S. Sakamoto, and F. Makkliang, "An eco-friendly method using deep eutectic solvents immobilized in a microcrystal cellulose-polyvinyl alcohol sponge for parabens analysis in food samples," *Microchem. J.*, vol. 191, p. 108758, 2023, doi: https://doi.org/10.1016/j.microc.2023.108758.

[132] L. Aljerf and A. Mashlah, "Characterization and validation of candidate reference methods for the determination of calcium and magnesium in biological fluids," *Microchem. J.*, vol. 132, pp. 411–421, 2017, doi: 10.1016/j.microc.2017.03.001.

[133] A. Gałuszka, P. Konieczka, and Z. M. Migaszewski, "Analytical Eco-Scale for assessing the greenness of analytical procedures," vol. 37, pp. 61–72, 2012, doi: 10.1016/j.trac.2012.03.013.

[134] F. Pena-pereira, W. Wojnowski, and M. Tobiszewski, "AGREE – Analytical GREEnness metric approach and software," pp. 0–28, 2020, doi:

10.1021/acs.analchem.0c01887.

[135] W. Nie *et al.*, “New method of aqueous two phase with solid phase extraction (ATP-SPE) for detection of sulfonamides,” *Microchem. J.*, vol. 150, no. July, p. 104076, 2019, doi: 10.1016/j.microc.2019.104076.

[136] D. Barzallo, E. Palacio, J. March, and L. Ferrer, “3D printed device coated with solid-phase extraction resin for the on-site extraction of seven sulfonamides from environmental water samples preceding HPLC-DAD analysis,” *Microchem. J.*, vol. 190, no. February, p. 108609, 2023, doi: 10.1016/j.microc.2023.108609.

[137] S. Hu *et al.*, “Nontargeted Screening and Determination of Sulfonamides: A Dispersive Micro Solid-Phase Extraction Approach to the Analysis of Milk and Honey Samples Using Liquid Chromatography-High-Resolution Mass Spectrometry,” *J. Agric. Food Chem.*, vol. 65, no. 9, pp. 1984–1991, 2017, doi: 10.1021/acs.jafc.6b05773.

[138] J. Huang *et al.*, “Determination of sulfonamides in food samples by membrane-protected micro-solid phase extraction coupled with high performance liquid chromatography,” *J. Chromatogr. A*, vol. 1219, pp. 66–74, 2012, doi: 10.1016/j.chroma.2011.11.026.

[139] H. Shaaban and T. Górecki, “Optimization and validation of a fast ultrahigh-pressure liquid chromatographic method for simultaneous determination of selected sulphonamides in water samples using a fully porous sub-2μm column at elevated temperature,” *J. Sep. Sci.*, vol. 35, no. 2, pp. 216–224, 2012, doi: 10.1002/jssc.201100754.

[140] K. W. Jung, S. Y. Lee, J. W. Choi, M. J. Hwang, and W. G. Shim, “Synthesis of Mg–Al layered double hydroxides-functionalized hydrochar composite via an in situ one-pot hydrothermal method for arsenate and phosphate removal: Structural characterization and adsorption performance,” *Chem. Eng. J.*, vol. 420, no. P1, p. 129775, 2021, doi: 10.1016/j.cej.2021.129775.

[141] L. D. Silva Neto, C. G. Anchieta, J. L. S. Duarte, L. Meili, and J. T. Freire,

“Effect of Drying on the Fabrication of MgAl Layered Double Hydroxides,” *ACS Omega*, vol. 6, no. 33, pp. 21819–21829, 2021, doi: 10.1021/acsomega.1c03581.

[142] I. Chouaybi, H. Ouassif, O. Matbout, M. Bettach, and E. M. Moujahid, “Highly Efficient Removal of Alizarin Yellow R Dye from Aqueous Solution Using a Synthetic Hydrocalumite-Type LDH (CaAl–NO3),” *J. Inorg. Organomet. Polym. Mater.*, vol. 33, no. 6, pp. 1517–1526, 2023, doi: 10.1007/s10904-023-02552-9.

[143] R. Pereira, A. Tojeira, D. C. Vaz, A. Mendes, and P. Bártolo, “Preparation and characterization of films based on alginate and aloe vera,” *Int. J. Polym. Anal. Charact.*, vol. 16, no. 7, pp. 449–464, 2011, doi: 10.1080/1023666X.2011.599923.

[144] I. Thermal and S. Characteristics, “Composite and Its Thermal Safety Characteristics,” 2022.

[145] F. L. Theiss, G. A. Ayoko, and R. L. Frost, “Thermogravimetric analysis of selected layered double hydroxides,” pp. 649–657, 2013, doi: 10.1007/s10973-012-2584-z.

[146] P. Karthikeyan and S. Meenakshi, “Environmental Chemistry and Ecotoxicology Development of sodium alginate @ ZnFe-LDHs functionalized beads : Adsorption properties and mechanistic behaviour of phosphate and nitrate ions from the aqueous environment,” vol. 3, pp. 42–50, 2021.

[147] A. L. Johnston, E. Lester, O. Williams, and R. L. Gomes, “Understanding Layered Double Hydroxide properties as sorbent materials for removing organic pollutants from environmental waters,” *J. Environ. Chem. Eng.*, vol. 9, no. 4, p. 105197, 2021, doi: 10.1016/j.jece.2021.105197.

[148] P. Del Gaudio, P. Colombo, G. Colombo, P. Russo, and F. Sonvico, “Mechanisms of formation and disintegration of alginate beads obtained by prilling,” *Int. J. Pharm.*, vol. 302, no. 1–2, pp. 1–9, 2005, doi: 10.1016/j.ijpharm.2005.05.041.

[149] T. S. Hussein and A. A. H. Faisal, “Nanoparticles of (calcium/aluminum/CTAB) layered double hydroxide immobilization onto iron slag for removing of cadmium ions from aqueous environment,” *Arab. J. Chem.*, vol. 16, no. 9, 2023, doi: 10.1016/j.arabjc.2023.105031.

[150] A. A. H. Faisal, Z. K. Ramadhan, N. Al-Ansari, G. Sharma, M. Naushad, and C. Bathula, “Precipitation of (Mg/Fe-CTAB) - Layered double hydroxide nanoparticles onto sewage sludge for producing novel sorbent to remove Congo red and methylene blue dyes from aqueous environment,” *Chemosphere*, vol. 291, no. October 2021, 2022, doi: 10.1016/j.chemosphere.2021.132693.

[151] V. V. Tolmacheva, V. V. Apyari, A. A. Furletov, S. G. Dmitrienko, and Y. A. Zolotov, “Facile synthesis of magnetic hypercrosslinked polystyrene and its application in the magnetic solid-phase extraction of sulfonamides from water and milk samples before their HPLC determination,” *Talanta*, vol. 152, pp. 203–210, 2016, doi: 10.1016/j.talanta.2016.02.010.

[152] M. H. Petrarca *et al.*, “Exploring miniaturized sample preparation approaches combined with LC-QToF-MS for the analysis of sulfonamide antibiotic residues in meat- and / or egg-based baby foods,” vol. 366, no. February 2021, 2022.

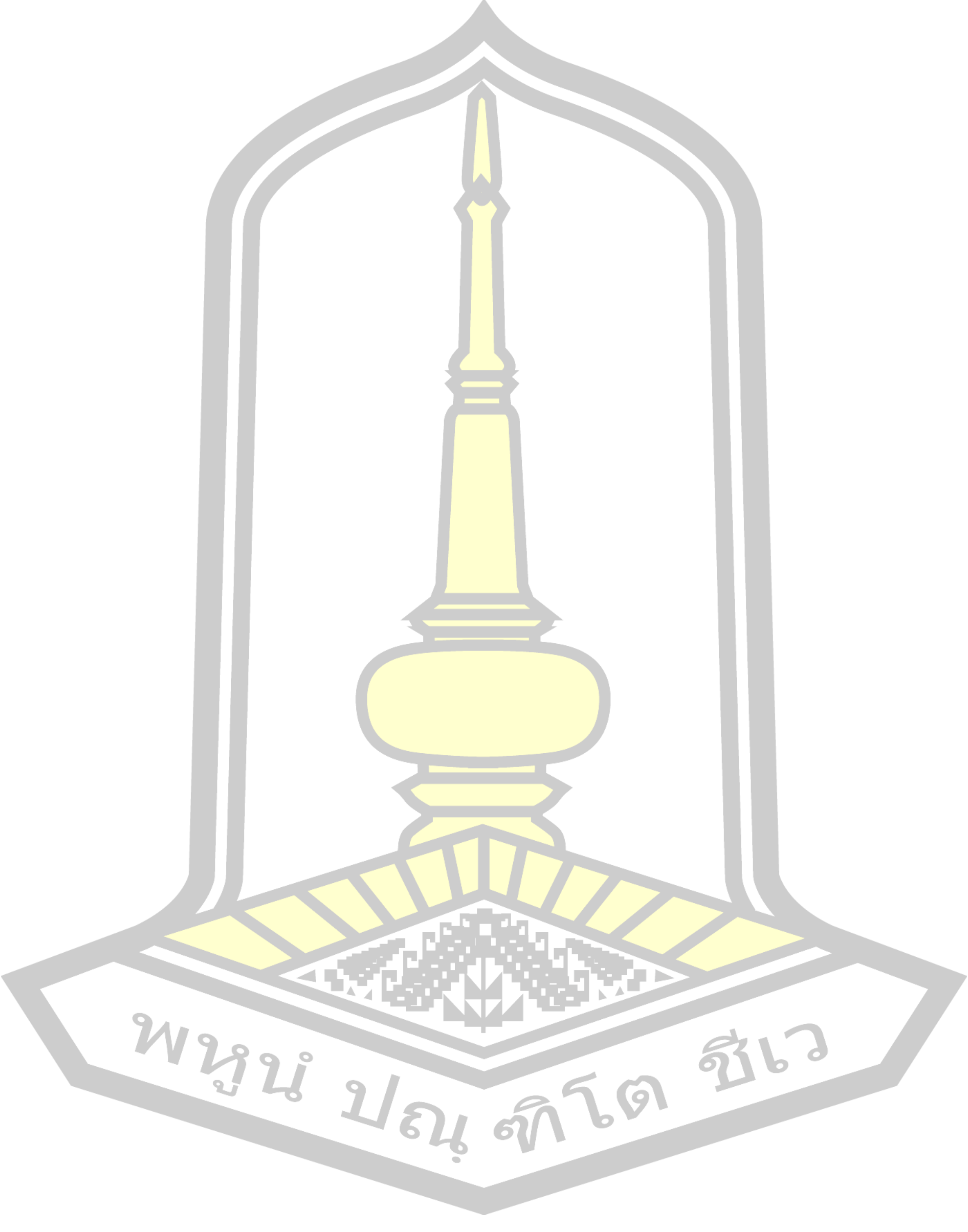
[153] I. S. Ibarra, J. M. Miranda, J. A. Rodriguez, C. Nebot, and A. Cepeda, “Magnetic solid phase extraction followed by high-performance liquid chromatography for the determination of sulphonamides in milk samples,” *FOOD Chem.*, vol. 157, pp. 511–517, 2014, doi: 10.1016/j.foodchem.2014.02.069.

[154] S. Sadeghi and S. Olieaei, “Nanostructured polyaniline based pipette tip solid phase extraction coupled with high-performance liquid chromatography for the selective determination of trace levels of three sulfonamides in honey and milk samples with the aid of experimental design met,” *Microchem. J.*, p. #pagerange#, 2019, doi: 10.1016/j.microc.2019.02.020.

[155] A. K. B. Iswas, G. S. R. Ao, N. K. Ondaiah, A. S. R. A. Njaneyulu, and J. K.

M. Alik, “Simple Multiresidue Method for Monitoring of Trimethoprim and Sulfonamide Residues in Buffalo Meat by High-Performance Liquid Chromatography,” pp. 8845–8850, 2007.

REFERENCES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