A magnetic hierarchical molecularly imprinted polymer nanocomposite adsorbent embedded with a zinc oxide carbon foam for the extraction of sulfonamides

Ananya Kliangsuwan

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry (International Program)
Prince of Songkla University
2022

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Author	Miss Ananya Kliangsuwan
Major Program	Chemistry (International Program)

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ร่วมกับนาโนซิงค์ออกไซด์คาร์บอนโฟมสำหรับการสกัดสารซัลโฟนาไมด์

ผู้เขียน นางสาวอนัญญา เกลี้ยงสุวรรณ

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บทคัดย่อ

วิทยานิพนธ์นี้มีจุดมุ่งหมายเพื่อพัฒนาตัวดูดซับชนิดใหม่ โดยใช้ตัวดูดซับอนุภาคแม่เหล็กเคลือบซิลิกาและซิงค์ออกไซด์คาร์บอนโฟมร่วมกับพอลิเมอร์ที่มีความจำเพาะสูง สำหรับสกัดเพื่อเพิ่มความเข้มข้นสารซัลโฟนาไมด์ในตัวอย่างนมและน้ำ โดยตรวจวิเคราะห์ด้วยเทคนิคโครมาโทกราฟีของเหลวสมรรถนะสูง ตัวดูดซับที่พัฒนาขึ้นอาศัยคุณสมบัติแม่เหล็กช่วยในการแยกตัวดูดซับจากตัวอย่างได้ง่ายและรวดเร็ว โดยอนุภาคแม่เหล็กขนาดนาโนเมตรเคลือบด้วยซิลิกาช่วยเพิ่มพื้นที่ผิวสำหรับการสกัดและคอมโพสิทร่วมกับซิงค์ออกไซด์คาร์บอนโฟมเพื่อเพิ่มอันตรกิริยาระหว่างซัลโฟนาไมด์และตัวดูดซับ ซึ่งสามารถเกิดอันตรกิริยาแบบ π-π และไฮโดรโฟบิก นอกจากนี้เพิ่มความจำเพาะเจาะจงสูงด้วยพอลิเมอร์ลอกแบบโมเลกุล การประยุกต์ใช้วัสดุเหล่านี้ร่วมกันส่งผลให้ประสิทธิภาพในการสกัดสูงขึ้น รวดเร็วและมีความจำเพาะเจาะจงต่อซัลโฟนาไมด์ ได้ศึกษาสภาวะที่เหมาะสม ได้แก่ ปริมาณของตัวดูดซับของแข็ง พีเอชของสารตัวอย่าง เวลาที่ใช้ในการสกัด ชนิดและปริมาณตัวทำละลายที่ใช้ชะสารตัวอย่างออกจากตัวดูดซับ เวลาที่ใช้ในการชะสาร และผลของเกลือ ภายใต้สภาวะที่เหมาะสม วิธีที่พัฒนาขึ้นให้ค่าช่วงความเป็นเส้นตรงที่ดีสำหรับการตรวจซัลโฟนาไมด์ตั้งแต่ 2.0 ถึง 150 ไมโครกรัมต่อลิตร มีขีดจำกัดการตรวจวัดเท่ากับ 2.0 ไมโครกรัมต่อลิตร ตัวดูดซับที่พัฒนาขึ้นมีประสิทธิภาพในการสกัดที่ดีโดยมีค่าร้อยละการได้กลับคืนอยู่ในช่วงร้อยละ 84.3 ถึง 96.2 และมีค่า

เบี่ยงเบนมาตรฐานสัมพัทธ์น้อยกว่าร้อยละ 7 ตัวดูดซับที่พัฒนาขึ้นมีข้อดีคือ มีความจำเพาะสูงและมีประสิทธิภาพในการสกัด ง่ายและสะดวก และความเสถียรที่ดีทำให้สามารถนำกลับมาใช้ซ้ำได้

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Abstract

This thesis aimed to develop a hierarchical nanocomposite adsorbent incorporated a zinc oxide and carbon foam embedded in a magnetic molecularly imprinted polymer (ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP). The adsorbent was utilized for the extraction and determination of sulfonamides. The fabricated adsorbent was characterized, the fabrication and extraction conditions were optimized and the extracted sulfonamides were determined using high performance liquid chromatography. The zinc oxide carbon foam helps to improve the adsorption of sulfonamides. The molecularly imprinted polymer provided highly specific recognition cavities for three sulfonamides and the magnetic material enabled the rapid isolation of the adsorbent after adsorption and desorption. Under optimum conditions, the developed method provided a good linearity from 2.0 to 150.0 μg L^{-1} with the coefficient of determination better than 0.995. The limit of detection and limit of quantification were 2.0 and 5.0 μg L^{-1}, respectively. The developed method was successfully applied to determine sulfonamides in milk and water samples with extraction recoveries between 84.3 and 96.2 % and RSDs lower than 7 %. The advantages of the developed nanocomposite adsorbent are high specificity and extraction efficiency, simplicity and convenience, and good stability that enables reuse.

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The successful accomplishment of this thesis would be impossible without the support and help of many people. I would like to show my deepest gratitude to those who have helped and supported me to complete this thesis.

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Ananya Kliangsuwan

The relevance of the research work to Thailand

The aim of this Master of Science Thesis in Chemistry (Analytical chemistry) was to develop and evaluate the performances of magnetite nanocomposite adsorbent, which was modified with amine, composited with carbon foam, and coated with molecularly imprinted polymer for the determination of sulfonamides in milk and water samples using high performance liquid chromatography coupled with diode array detector (HPLC-DAD).

This developed adsorbent has several advantages including high extraction efficiency and useful for the simultaneous extraction and determination of sulfonamides in milk and water samples. It can be used by several government agencies in Thailand, the Ministry of Public Health, Ministry of Environment and the Ministry of Education.

Contents

Contents (Continued)

List of tables

List of tables (Continued)

List of figures

Figure **Page**

List of figures (Continued)

Figure **Page**

List of figures (Continued)

Figure **Page**

List of abbreviations

ACN	Acetonitrile
APTES	Alpha-azo-isobutyronitrile
BET	Brunauer-Emmett-Teller
EGDMA	Ethylenegylcoldimethacrylate
EU	European union
FESEM	Field emission scanning electron microscopy
FTIR	Fourier transform infrared spectroscopy
HPLC	High-performance liquid chromatography
LOD	Limit of detection
LOQ	Limit of quantification
MAA	Methacrylic acid
MIP	Molecularly imprinted polymer
MRLs	Maximum residue limits
MSPE	Magnetic solid phase extraction
NIP	Non-imprinted polymer
R^2	Coefficient of determination
RSD	Relative standard deviation
SDZ	Sulfadiazine
SDM	Sulfadimethoxine
SMT	Sulfamethazine
UV - VIS	Ultraviolet - visible
VSM	Vibrating sample magnetometer

List of publication

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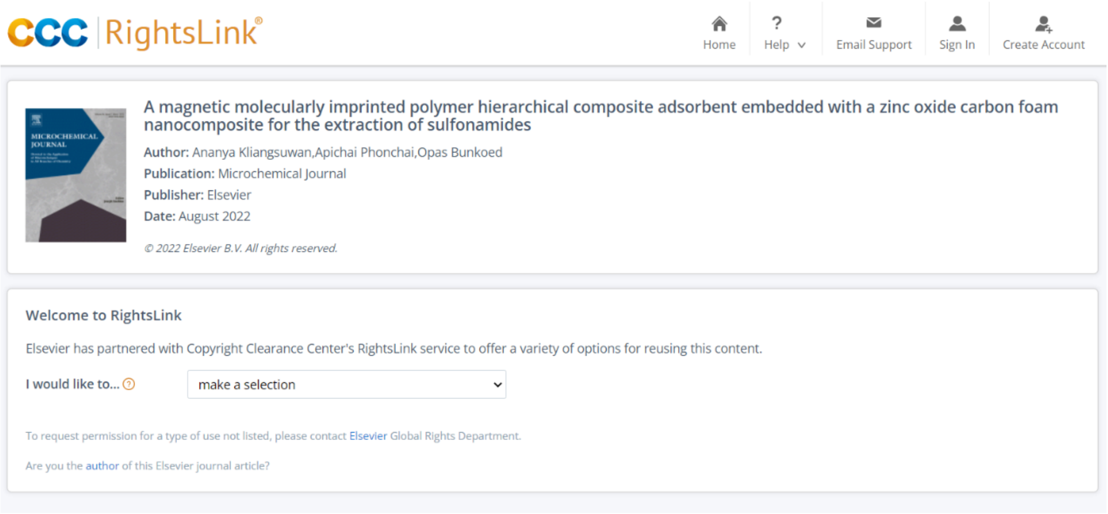

A magnetic molecularly imprinted polymer hierarchical composite adsorbent embedded with a zinc oxide carbon foam nanocomposite for the extraction of sulfonamides

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1. Introduction

1.1. Background and rationale

Sulfonamides are widely used as veterinary antibiotics to prevent infectious bacterial diseases and to support animal husbandry and fish farming (Shi et al., 2011). The existence of residual sulfonamides in animal products and the environment is an unavoidable result of the wide usage of these antibiotics. The adverse effects of sulfonamides on humans can cause allergic reactions, damage to the urinary system and inhibition of leukocyte generation. Owing to the long-term and excessive usage of sulfonamides, the accumulation of residues in the food chain is becoming an increasingly serious problem (Ayankojo et al., 2020). Sulfonamides have been continuously employed in animal husbandry and fish farming such as sulfadiazine (SDZ), sulfamethazine (SMT) and sulfadimethoxine (SDM) because of their cost effectiveness and broad antibacterial spectrum. Therefore, the determination of sulfonamides residue in food products and environment is an importance.

Several methods have been reported for the determination of sulfonamides such as chromatographic techniques (Charitonos et al., 2017; Sukchuay et al., 2015; Yazdanfar et al., 2021), fluorescence spectroscopy (Orachorn & Bunkoed, 2021), UV-Vis spectroscopy (Shakirova et al., 2021) and electrochemical sensors (Li & He, 2021; Melo Henrique et al., 2021). Among these methods, high performance liquid chromatography (HPLC) is the most widely used. Since HPLC uses an analytical column to separate analytes before quantification. However, residual sulfonamides in food and environment are normally at trace levels which cannot be directly determined by instrumental analysis. Therefore, the sample preparation is recommended to preconcentrate the analyte and to remove the interferences prior to instrumental analysis. Several sample preparation method were used for the extraction of sulfonamides including solid phase extraction (SPE) (Moga et al., 2020; Wen et al., 2020), liquid–liquid microextraction (LLME) (Shakirova et al., 2021), deep eutectic solvents (DESs) (Shishov et al., 2020) and magnetic solid-phase extraction (MSPE) (Sukchuay et al., 2015). MSPE is a simple and rapid procedure (Jullakan & Bunkoed, 2021) which avoids the problems of conventional SPE, which is usually time-consuming and requires complicate manifold system.

The extraction efficiency of target analytes is normally depends on the effectiveness of the adsorptive material. Various materials have been utilized to extract sulfonamides including carbon nanotubes (Zheng et al., 2021), polypyrrole (Sukchuay et al., 2015), covalent organic frameworks (Zhang et al., 2020), functionalized ionic liquids-supported metal organic frameworks (Lu et al., 2020), poly(ethylene glycol) diacrylate (Moga et al., 2020), molybdenum disulfide nanosheets (Li Juan et al., 2020) and graphitic carbon (Liu et al., 2020). An interesting material for the extraction of sulfonamides in complex samples is molecularly imprinted polymer (MIP). MIPs are highly specific to target analytes and can reduce the co-adsorption of interferences in real samples. In addition, MIPs are easily synthesized and chemically stable.

MIPs can be integrated with other materials to produce a composite adsorbent with improve affinity for the target analytes. Zinc oxide (ZnO) has been reported to effectively extract sulfonamides. However, it has poor dispersibility and readily aggregates (Zhang et al., 2016). ZnO incorporated with carbon foam is more interesting material that has shown exciting potential for the extraction of target compounds since it has a specific pore structure, a highly geometric surface area and good thermal stability. This composite material can adsorb sulfonamides via hydrophobic and π-π interactions and hydrogen bonding. The specificity of a MIP adsorbent can be improved by incorporating ZnO@Carbon foam.

In this work, a hierarchical nanocomposite magnetic adsorbent was fabricated by integrating a ZnO@Carbon foam nanocomposite and magnetite nanoparticles (Fe_3O_4) with a molecularly imprinted polymer (ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP). The developed hierarchical nanocomposite adsorbent was characterized and the fabrication strategy and extraction condition were optimized. The developed adsorbent was applied as the dispersive magnetic solid phase extraction (d-MSPE) of sulfonamides in milk and water samples. The extraction efficiency of the developed adsorbent was also compared with a commercial sorbent for the extraction of three sulfonamides, sulfamethazine (SMT), sulfadiazine (SDZ), and sulfadimethoxine (SDM).

1.2. Objective

To develop a selective and high extraction efficiency adsorbent using magnetic hierarchical molecularly imprinted polymer nanocomposited with zinc oxide carbon foam (ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP) for the extraction and preconcentration of sulfonamides.

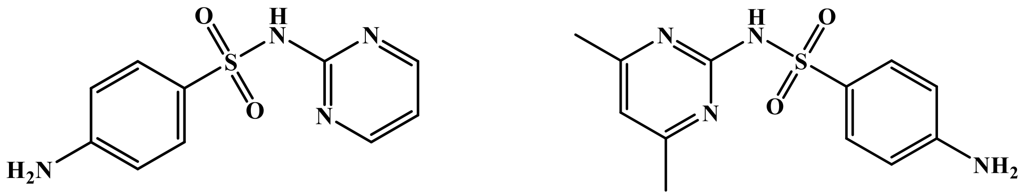
1.3. Chemical properties and toxicity of sulfonamides

Sulfonamides (SAs) are broad-spectrum antibiotics (**Fig. 1.1**), which widely used in animal husbandry and aquaculture, they can prevent or treat 30 bacterial infections (Lin et al., 2020). Sulfonamides are utilized in animal production, and an estimated 60% of livestock have been exposed to them. The expanding use of sulfonamides in medical treatments and animal farming, along with poor waste management procedures, resulted in major environmental issues as residues (Rozaini et al., 2019). Antibiotics can transfer to human bodies through consumption of milk and residues in aquaculture water.

Among those types of sulfonamides, sulfadiazine, sulfamethazine and sulfadimethoxine have been mostly used in treating diseases. Sulfadiazine, a sulfa drug, eliminates bacteria that cause infections, especially urinary tract infections. Sulfamethazine is used for pneumococcal, staphylococcal, and streptococcal infections as well as for sepsis, gonorrhea and other infectious diseases. Sulfadimethoxine is used almost exclusively for the treatment of intestinal parasites known as *Coccidia* (Ji et al., 2017).

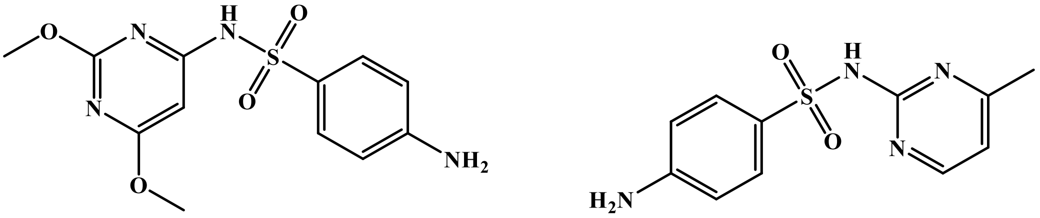
According to the Food and Drug Administration (FDA) report, there are several diseases that have been treated by sulfonamides. Sulfonamide residues in the human body lead to allergic sensitization and invasive growth of tumor cells through one or several mechanisms, which make sulfonamides ineffective in the treatment of several diseases in the long term.

However, sulfonamides have some disadvantages regarding to their toxicity. European Commission has released a rule which is about the maximum residue level of sulfonamides in animal tissue which is stated in Commission Regulation (EU) No 37/2010. The maximum residue levels of sulfonamides in food products are shown in **Table 1**. Some researchers have studied about the toxic effect of sulfonamides for the human body. The effect includes hemolytic anemia, leukopenia and thrombocytopenia may occur. The most important organ affected in toxicity is the kidney. The patient had some symptoms such as dizziness, diarrhea, nausea, vomiting and serious skin rashes (Kester, Karpa, & Vrana, 2012).



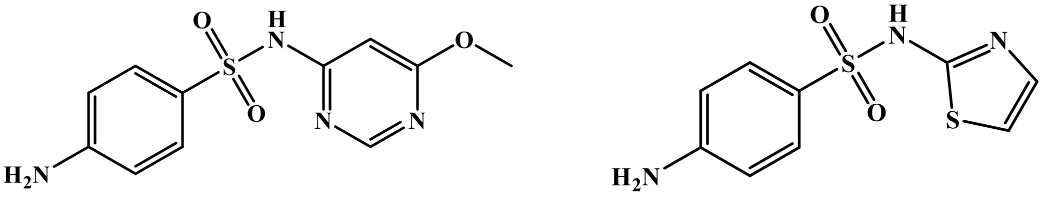
Sulfadiazine, SDZ

Sulfamethazine, SMT



Sulfadimethoxine, SDM

Sulfamerazine, SME



Sulfamonomethoxine, SMM

Sulfathiazole, STZ

Figure 1.1 Chemical structure of sulfonamides

Table 1. The maximum residue level of sulfonamides in food animal products

Animal species	MRL (µg kg^{-1})	Target tissue
All food producing species	100	Muscle Fat Liver Kidney
Bovine Ovine Caprine	100	Milk

1.4. High performance liquid chromatography (HPLC)

HPLC has been widely utilized for the quantification of sulfonamides due to its high sensitivity and good precision (Lin et al., 2020). HPLC is a separation technique based on the distribution of analytes between a stationary phase and mobile phase using high pressure to push through the column. Revered phase HPLC is typically used for the separation and determination of sulfonamides. This mode use of a polar mobile phase and a non-polar stationary phase. The separation time depend on the type of stationary phase, the chemical property of the analytes, the molecules are retarded in column and passed to detector. The signals are converted and recorded by computer software. A schematic of a typical HPLC system is showed in **Fig. 1.2.**

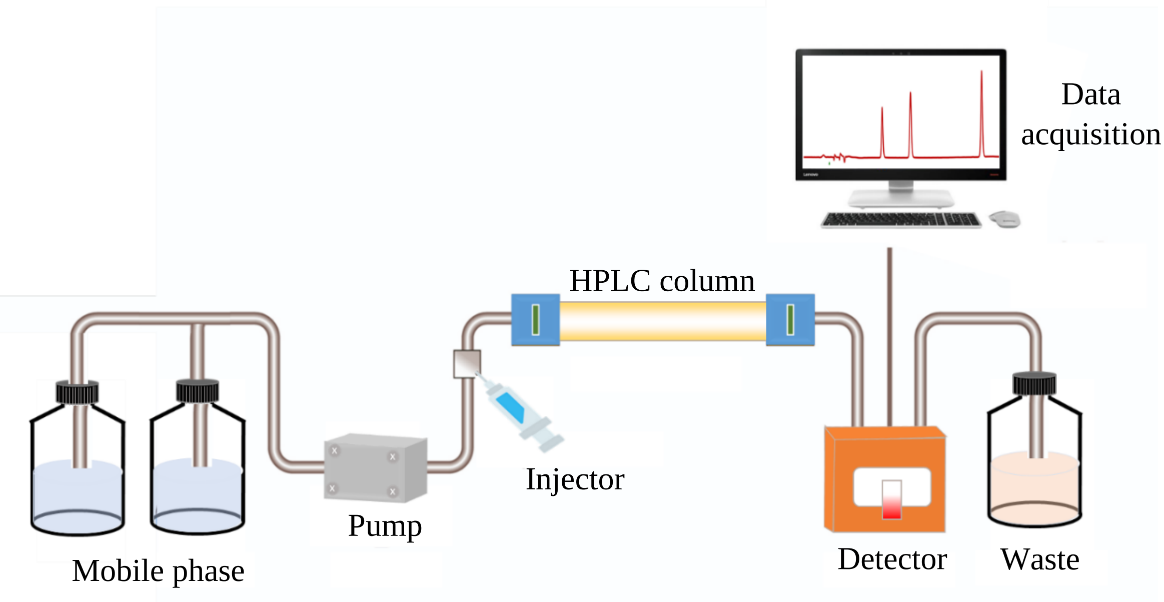


Fig. 1.2 A schematic of an HPLC system

To obtain the best performance including good sensitivity and separation, and short analysis time some parameters of HPLC system must be investigated including the mobile phase composition, flow rate of mobile phase and detection wavelength. The mobile phase composition relies on the polarity of the analytes and the HPLC mode. The suitable mobile phases for the separation of sulfonamides are shown in **Table 2.**

The stationary phase is a vital part for the separation of target analytes in complex mixtures and its selection is an important for the good result of the analysis which are work together with the mobile phase to pass through the system. Several types of stationary phase were reported for the separation and determination of sulfonamides including octadecyl (C18) which is dependent on the contact surface area between the nonpolar moiety of the target analytes and the stationary phase. In this study, the separation column was a Fortis^{TM} RP C18 (4.6 x 150 mm I.D., 5.0 µm particle size) and contain octadecyl modified silica which were used for the separation of sulfonamides are shown in **Table 2.**

The detector was used for the identification of analytes. It is based on specific property of analytes, composition of mobile phase and sample which signal response to a specific compound. There are several detectors available for the quantification of sulfonamides such as ultraviolet (UV) (Shi et al., 2011), diode-array detector (DAD) (Qi et al., 2015), fluorescence (FLD) (Patyra et al., 2019) and mass spectrometer (MS) (Yao & Du, 2020).

Diode array detector (DAD) is commonly used in liquid chromatography. DAD had a wide range of wavelengths to screening for many drugs and toxic substances and ability to select the best wavelength for analysis. In addition, DAD had some advantages such as sensitive and selective for the detection of many compounds (Xia et al., 2020). In this work, the diode array HPLC detectors was used for analysis of sulfonamides since it was selective, sensitive and reliable detector.

Table 2. Mobile phase composition for the separation and determination of sulfonamides

Column	Mobile Phase	Flow Rate (mL/min)	Detection (UV) nm	References
C_{18}	0.5% sodium dihydrogen phosphate aqueous solution -ACN (85:15, v/v)	2.0	270	(Yao & Du, 2020)
CTO 20AC	Water: ACN containing 0.1% (v/v) formic acid	1.0	200 – 360	(Chatzimitakos & Stalikas, 2020)
Ultimate AQ-C_{18}	ACN: water (30:70, v/v)	1.0	270	(Li et al., 2018)
C_{18} Kromasil	Water containing 1% HAcO (pH = 3.2) and ACN with 1% HAc	1.0	280	(Ancuta Moga et al., 2020)
C_{18} Hichrom	Methanol: water adjusted to pH = 3	1.0	262	(Sadeghi & Olieaei, 2019)
Hypersil gold	Water: ACN (5:95, v/v)	1.0	270	(Xia et al., 2020)
Zorbax SB-C_{18}	Water with 1% acetic acid at pH 4.0: ACN (75:25, v/v)	1.0	269	(Nasir et al., 2019)
SUPELCO C_{18}	0.75% formic acid: mixture of ACN and methanol at a ratio of 2:1	1.0	257	(Bogdanova et al., 2020)
Replete RPL-D2000	ACN: methanol (8:92, v/v)	1.0	265	(Mokhtar et al., 2019)
InertSustain C_{18}	Methanol: 0.01 mol L^{-1} oxalic acid in water (32:68, v/v)	0.7	-	(Lu et al., 2020)

1.5. Sample preparations

Sample preparation is an important step for the detection of sulfonamides in various matrices. The aims for doing sample preparation are to clean-up and preconcentrate the target analytes in complex matrices to reach low detection limit (Feng et al., 2016). There are several things that should be considered in sample preparation such as the degree of selectivity, the time consuming for sample preparation, enhances extraction efficiency and simple to carry out (Yang et al., 2019). Sample preparation is needed for the determination of sulfonamides due to its existence in trace level. Several sample preparation techniques have been developed for the extraction and preconcentration of sulfonamides in various samples (**Table 3**).

1.5.1 Liquid liquid extraction (LLE)

Liquid liquid extraction (LLE) is based on the principle that a solute or an analyte can distribute itself in a certain ratio between two immiscible solvents, usually water (aqueous phase) and organic solvent (organic phase). LLE is widely used in sample preparation for cleanup and enrichment, which results in signal enhancement (Su et al., 2017). However, there are some drawbacks such as often cumbersome and time-consuming, especially requires large amounts of organic solvents which pose health and environmental hazards (Di et al., 2019).

1.5.2 Solid phase extraction (SPE)

The basic principle of SPE is the partitioning of compounds between two phases of solid and liquid. The target analytes must be greater affinity to the solid phase than for the sample matrix. The compounds retained (analytes) on the solid phase can be removed by eluting solvent with a greater affinity (Mukherjee, 2019). SPE procedures are basically consist of four steps including conditioning, sample loading, washing and eluting **(Fig. 1.3)**. The SPE method has attracted increasing attention in the separation and purification of real samples due to the advantages of high recovery and simple operation.

SPE can reduce time and solvent required, manage with a small amount of samples and solvent compared to liquid liquid extraction (Salehi et al., 2016)

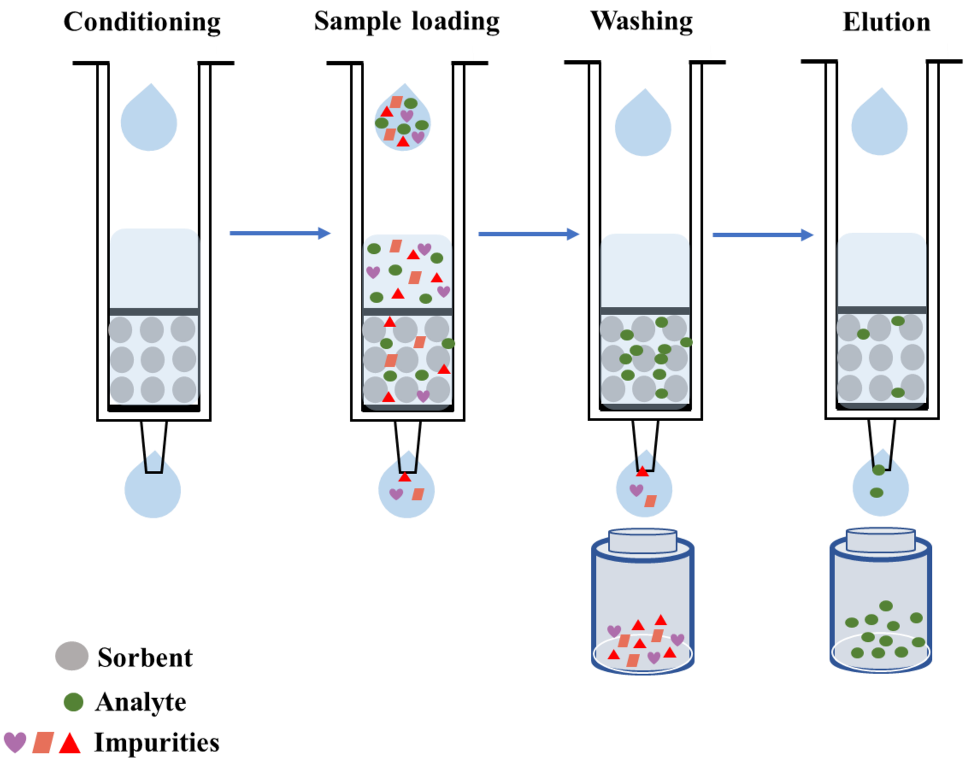


Figure 1.3 Schematic representative the solid phase extraction procedure

1.5.3 Magnetic solid phase extraction (MSPE)

MSPE is a new mode of SPE, which based on the application of magnetic adsorbents. A magnetic adsorbent takes an important role in the MSPE procedure (Wang et al., 2019). MSPE is superior to SPE, such as being time saving (Mohamed et al., 2019). The adsorbents do not need to be packed into a cartridge (as in traditional SPE) and their separation can be easily achieved using an external magnet located outside the extraction vessel, thus avoiding the need for centrifugation or filtration makes the sample preparation easier and faster (Herrero et al., 2015). However, because of the large number of active ingredients in food and the low concentration of residual antibiotics. To overcome these problems, molecularly imprinted polymer (MIP) is an alternative material that composited into adsorbent to increase selectivity and high affinity.

1.5.4 Molecularly imprinted polymer

MIPs are synthetic polymers with a predetermined selectivity for a given analyte, or group of structurally related compounds, making them ideal materials to be used in separation processes (Turiel & Esteban, 2020). MIPs provides some advantages such as selective recognition of template in the presence of structural analogues, rapid separation from complex matrix under an external magnetic field, high binding capacity and outstanding adsorption (Zhong et al., 2018).

MIPs are widely used in the sample preparation techniques such as solid phase extraction (SPE) (Cheng et al., 2021), dispersive micro solid phase extraction (D-µ-SPE) (Jalilian et al., 2021), stir bar sorptive extraction (SBSE) (Tang et al., 2018), magnetic solid phase extraction (MSPE) (Liang et al., 2020). MIPs can be integrated with other materials to produce a composite adsorptive material with improve affinity for the target analytes. It can prevent the magnetic nanoparticles from aggregation and increase the selectivity of magnetic nanoparticles (Du et al., 2018). The co-polymerization method involves a functional monomer, a crosslinker, and a molecular template. In the imprinted binding sites, the functional monomers are in charge of the binding interactions. The cross-linker in the polymer network's function is to organize the monomer into specific sites and orientations around the template molecules, hence maintaining the binding site structure (specific cavities). During template removal, the polymer contains cavities that are similar to template molecules in size, shape, and functional group (**Fig. 1.4**). In addition, the benzene rings within MIP-MSPE and sulfonamides would induce π-π interaction. This is an attractive strategy for this work. Zinc oxide (ZnO) has been reported to effectively extract target compounds. However, it has poor dispersibility and readily aggregates (Zhang et al., 2016). ZnO incorporated with carbon foam is a more interesting material that has shown exciting potential for the extraction of target compounds since it has a specific pore structure, a highly geometric surface area and good thermal stability. This composite material can adsorb sulfonamides via hydrophobic, π-π interactions and hydrogen bonding. The specificity of an MIP adsorbent can be improved by incorporating ZnO@Carbon foam. The interaction between target analytes and developed adsorbent are presented in **Fig. 1.5**

In this work, a hierarchical nanocomposite magnetic adsorbent was fabricated by integrating a magnetite nanoparticle (Fe_3O_4) and ZnO@Carbon foam nanocomposite to increase surface area. After that, MIPs was coated on the surface of magnetite for the selective determination of sulfonamides in samples.

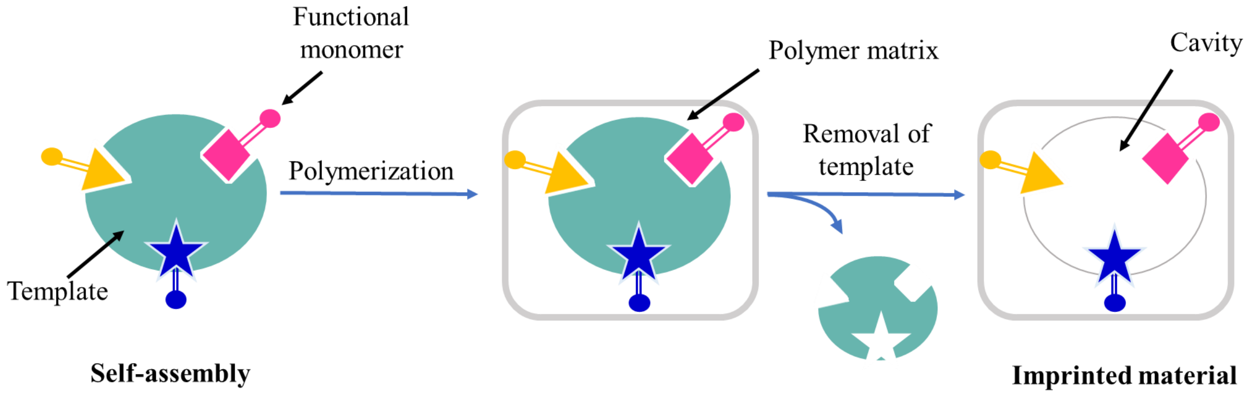


Figure 1.4 The molecularly imprinting polymer process

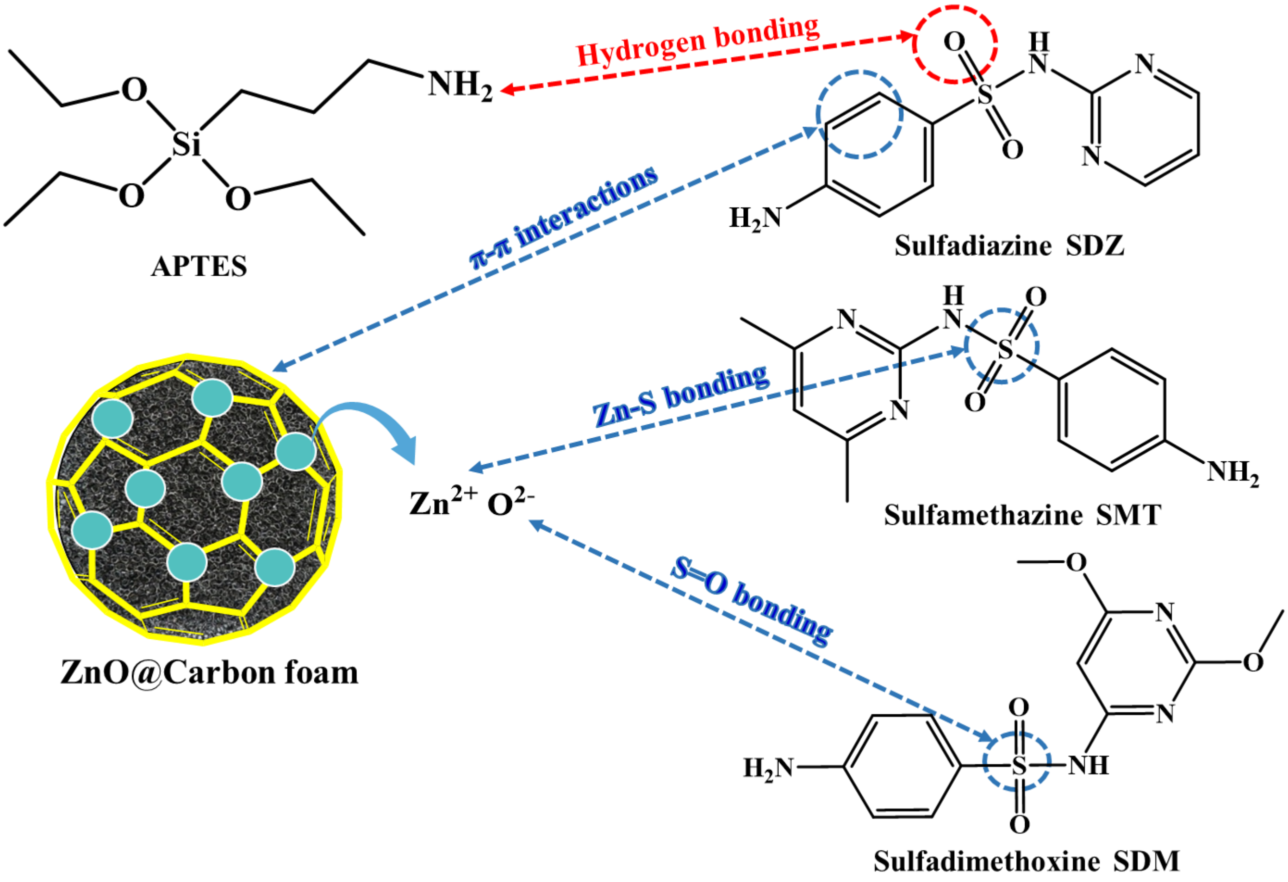


Figure 1.5 The interaction between target analytes and developed adsorbent

Table 3. Sample preparation techniques for the determination of sulfonamides

Extraction method	Sample	Extraction time (min)	Sample volume (mL)	Extractant	LOD	Recovery (%)	References
Solid phase extraction (Molecularly imprinted solid phase extraction, MISPE, 25 mg)	Shrimp fish	-	10	Methanol/acetic acid (9:1, v/v)	8.4 – 10.9 µg kg^{-1}	85.5 - 106.1	(Shi et al., 2011)
Solid phase extraction (Molecularly imprinted solid phase extraction, MISPE, 20 mg MIP)	Lake river	-	50	Methanol	0.010 – 0.014 µg L^{-1}	87.4 – 102.3	(Fan et al., 2020)
Solid phase dispersion (Matrix solid phase dispersion, MSPD, 50 mg)	Pork	3	-	Methanol/acetic acid (9:1, v/v)	0.5 – 3.0 ng g^{-1}	74.5 – 102.7	(Wang et al., 2017)
Molecularly imprinted silica gel, MISG (MISG, 15 mg)	Tap river	10	12.5	5% ammonia in ACN	0.06 – 0.17 µg L^{-1}	80.0 – 96.0	(Rozaini et al., 2019)
Solid phase dispersion (Molecularly imprinted polymer solid phase dispersion, MIP-SPE, 50 mg)	Animal-derived water	-	25	Water	0.02 – 0.1 µg L^{-1}	63.5 – 115.7	(Zhao et al., 2018)
Dispersive solid phase extraction (MIL-101(Cr)@GO, 5 mg)	Milk	20	1	Water	0.012 – 0.145 µg L^{-1}	79.8 - 103.8	(Jia et al., 2017)
Solid phase dispersion (Magnetic graphene oxide nanoparticles, MSPE-CMGO, 15 mg)	Waterwork outlet aquaculture water	20	200	Methanol	0.49 – 1.59 ng L^{-1}	82.0 – 106.2	(Gao et al., 2018)
Ultrasound-assisted dispersive micro solid phase extraction (20 mg of zinc ferrites)	Egg lake water	30	20	ACN/ formic acid (8:2, v/v)	0.06 – 0.11 µg L^{-1}	88.0 – 101.0	(Chatzimitakos & Stalikas, 2020)
Aqueous two-phase sample pretreatment method with solid phase extraction (ATP-SPE, HLB)	Fish tissue	-	10	Methanol	5.8 – 11.7 ng g^{-1}	80.1 – 95.1	(Yao & Du, 2020)

2. Research Methodology

2.1 Chemical and reagents

Iron (II) chloride tetrahydrate and iron (III) chloride hexahydrate were from Sigma Aldrich (Steinheim, Germany). Sucrose was obtained from Ajax Finechem (Australia). Zinc nitrate hexahydrate was from KEMAUS (Australia). Sulfamethazine (SMT), sulfadiazine (SDZ), sulfadimethoxine (SDM), ethylene glycol dimethacrylate (EGDMA), methacrylic acid (MAA), and 3-aminopropyltriethoxysilane (APTES) were purchased from Tokyo Chemical Industry Co. Ltd (Tokyo, Japan). Acetonitrile was from Merck (Darmstadt, Germany). Alpha-azoisobutyronitrile (AIBN) was from BDH Chemicals (Lutterworth, UK). Acetone, ethanol, acetic acid, and methanol were from RCI Labscan (Bangkok, Thailand).

2.2 Instrumentation

The HPLC analysis was performed in gradient mode on an 1100 series HPLC system (Agilent Technologies, Waldbronn, Germany) equipped with a C18 (4.6 x 150 mm I.D., 5.0 µm) analytical column for the separation of target sulfonamides. The mobile phase was acetonitrile and 0.02 % (v/v) acetic acid at a flow rate of 1.0 mL min^{-1}. The injection volume was 20 µL and the target sulfonamides were detected at 270 nm. The morphology of the adsorbent was examined by field emission scanning electron microscope (FESEM), (Apreo FEI, Netherlands). The infrared spectra of the adsorbent and related materials were recorded by Fourier transform infrared spectrometer (Bruker, Germany). The crystalline phases of the adsorbent were determined by X-ray diffractometer (XRD) (Empreyan, PAN analytical, the Netherlands). Magnetic properties were determined with vibrating sample magnetometer (VSM) calibrated with a 3 mm diameter Ni sphere (Lakeshore 730908, USA). The specific surface areas were determined by a Brunauer–Emmett–Teller (BET) surface area and pore size analyzer (Model ASAP 2060 Micromeristic, USA).

2.3 Preparation of composite magnetic solid phase extraction adsorbent

2.3.1 Synthesis of Fe_3O_4-SiO_2-NH_2 nanoparticles

Fe_3O_4 nanoparticles were synthesized via a co-precipitation method in accordance with a previous report (Kaewsuwan et al., 2017). Briefly, 3.40 g of $FeCl_2 \cdot 4H_2O$ and 9.40 g of $FeCl_3 \cdot 6H_2O$ were dissolved in 150 mL of deionized (DI) water and transferred into a three-necked flask (250 mL). The solution was stirred under nitrogen at 80 °C for 10 min and then 20 mL of ammonium hydroxide were added dropwise and stirring proceeded continuously for 1 h, at which point Fe_3O_4 nanoparticles were obtained. The nanoparticles were separated with a magnet, washed with 50 mL of DI water and dried at 70 °C for 5 h.

The Fe_3O_4-SiO_2-NH_2 nanoparticles were prepared by dispersing 0.50 g of the Fe_3O_4 nanoparticles in a 90 mL mixture solution of ethanol and deionized water (1:1 v/v) under ultrasonication for 30 min. Then, 0.70 mL of APTES was added and adjusted to pH 4 with 1.0 M acetic acid. The reaction was performed for 3 h under stirring at 60 °C. The synthesized Fe_3O_4-SiO_2-NH_2 nanoparticles were separated with an external magnet, washed with 50 mL DI water and dried at 80 °C for 8 h.

2.3.2 Synthesis of zinc oxide incorporated carbon foam (ZnO@CF)

The ZnO@CF composite was synthesized according to a previous method (Sajid et al., 2016). Briefly, 3.0 g of sucrose and 1.5 g of $Zn(NO_3)_2 \cdot 6H_2O$ were combined in a beaker and heated to 110°C. As the temperature increased, the mixture started to melt. During melting, the mixture was continuously stirred with a glass rod and started to turn yellow, expand and foam. After further heating for approximately 10 min at 110°C, the foam turned black and the ZnO@CF composite was obtained. The synthesized ZnO@CF was stored in a desiccator until used.

2.3.3 Synthesis of magnetic molecularly imprinted polymer (MMIPs)

For the synthesis of magnetic molecularly imprinted polymer, 0.019 g, 0.017g and 0.015 g of sulfadimethoxine, sulfamethazine and sulfadiazine were dispersed in 60 mL of acetonitrile, respectively. Then, 90 µL of methacrylic acid was added into dispersion solution and stirred for 12 h at room temperature. After that, 0.10 g of $Fe_3O_4@SiO_2-NH_2$ and 0.050 g of ZnO@CF were added into the solution. The incubate solutions were moved to three neck flask. Then, 3.8 mL of ethylene glycol dimethacrylate (EGDMA) was added following by 0.0750 g of 2,2 azobisisobutyronitril (AIBN). The polymerization was performed under N_2 at 60°C for 24 h. The obtained MMIPs were washed with a mixture of MeOH: acetic acid (8:2, v/v) and sonicated until no sulfonamides were detected and washed with deionize water. The obtained nanoparticles were dried in an oven at 80°C for 8 h.

The magnetic non-imprinted polymers (MNIPs) were synthesized using the same method as MMIPs but without the existence of analyte (sulfonamides). The preparation procedure of magnetic molecularly imprinted polymer is showed in **Fig. 2.1.**

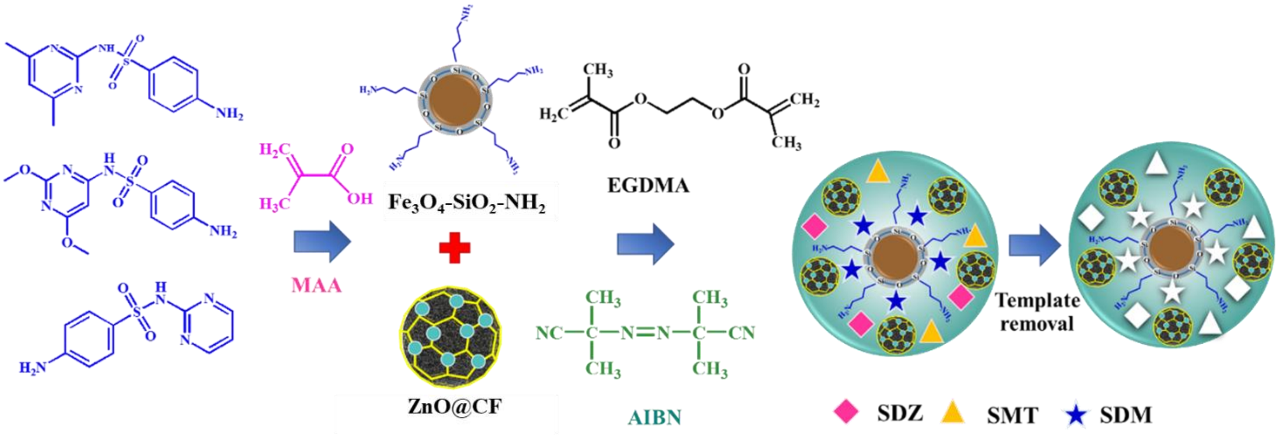


Fig. 2.1 The preparation procedure of the hierarchical nanocomposite $ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP$ adsorbent for the extraction of sulfonamides

2.4 Dispersive magnetic solid phase extraction (d-MSPE) procedure

The d-MSPE extraction of sulfonamides using the fabricated adsorbent is showed in **Fig. 2.2**. 50 mg of the adsorbent were dispersed in 15.0 mL of sample solution and stirred at 750 rpm for 30 min. After the adsorption of sulfonamides was completed, the adsorbent was separated from the sample solution using a magnet. The adsorbent particles were placed in 2.0 mL of a desorption solution of methanol and 1.0 M acetic acid (80:20 % v/v) and the adsorbed analytes were desorbed under ultrasonication for 30 min. The adsorbents were separated with the magnet and the desorption solution was evaporated to dryness at 50 °C. Finally, the residue was dissolved in 1.0 mL of mobile phase and 20 μL was injected into the HPLC-DAD system for analysis.

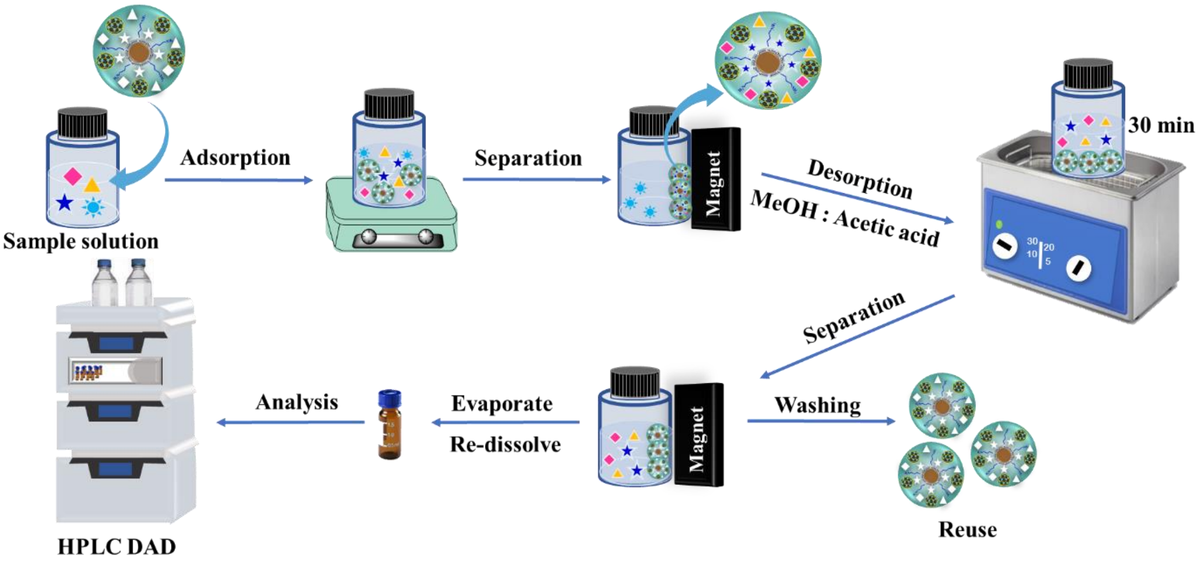


Fig. 2.2 Magnetic solid phase extraction procedure using MMIPs for the extraction of sulfonamides

3. Results and discussion

3.1. HPLC condition

The HPLC condition was investigated for the analysis of sulfonamides and the suitable condition is shown in **Table 4.** To obtain the best performance including good separation, short analysis time and high sensitivity, a gradient system of mobile phase was performed for sulfonamides analysis. The mobile phase was acetonitrile and 0.02 % (v/v) acetic acid at a flow rate of 1.0 mL min^{-1}. The injection volume was 20 µL and the target sulfonamides were detected at 270 nm. The total analysis time of three sulfonamides is about 12.0 min with good separation of sulfadiazine, sulfamethazine and sulfadimethoxine with retention times of 4.51, 6.04 and 9.88 min, respectively (**Fig 3.1**).

Table 4 HPLC condition for the analysis of sulfonamides

Parameters	Conditions
Column	Fortis^{TM} C18 column (4.6 x 150 mm I.D., 5.0 µm particles size)
Flow rate	1.0 mL min^{-1}
Mobile phase	Acetic acid 0.02% (v/v) (A) and acetonitrile (B)
Gradient system	0 min = 22.0 % B, 5.0 min = 35 % B, 8.0 min = 45 % B, 10.0 min = 35 % B, 12.0 min = 22 % B
Detector	Diode array detector (λ = 270 nm)
Injection volume	20 µL
Column temperature	30 ^{o}C

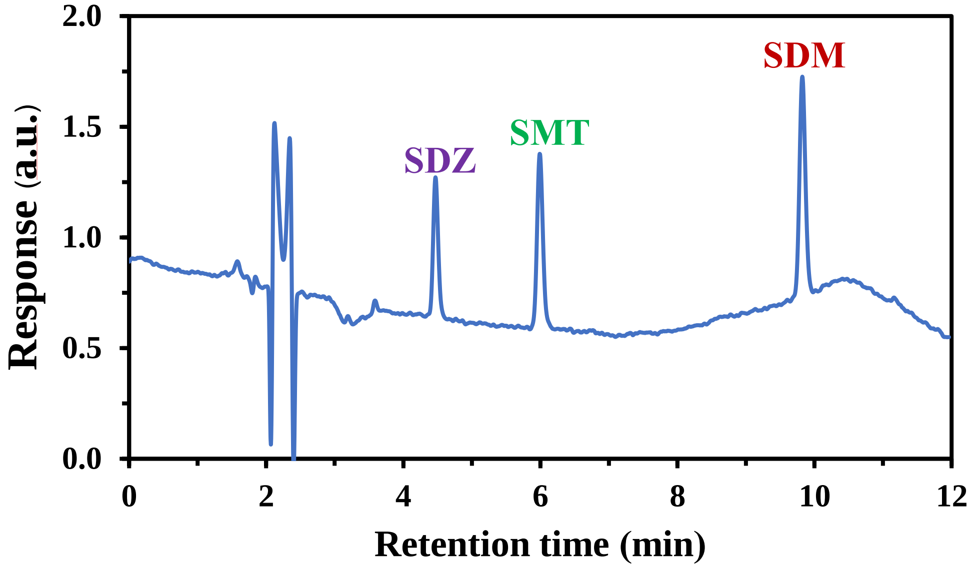


Fig. 3.1 Chromatograms of sulfadiazine (SDZ), sulfamethazine (SMT) and sulfadimethoxine (SDM) (75 µg L^{-1})

3.2 The characterization of magnetic molecularly imprinted polymer adsorbent

The functional groups of ZnO@CF, Fe_3O_4-SiO_2-NH_2 and the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent were investigated using FT-IR analysis. The FT-IR spectrum of ZnO@CF (**Fig. 3.2a**), shows a peak at 758 cm^{-1} from the Zn–O stretching vibration and a peak at 2952 cm^{-1} corresponding to the C–H bond vibration of carbon foam. These peaks confirm that ZnO@CF was successfully synthesized. The FT-IR spectrum of Fe_3O_4-SiO_2-NH_2 nanoparticles (**Fig. 3.2b**) presents an adsorption peak at 588 cm^{-1} due to the stretching of Fe-O, a peak at 1622 cm^{-1} corresponding to –NH_2 stretching vibration, a peak at 1094 cm^{-1} from the stretching vibration of the Si–O–Si bond, and a peak at 3394 cm^{-1} corresponding to the stretching of the O–H bond. These characteristic peaks confirmed that the magnetic Fe_3O_4-SiO_2-NH_2 nanoparticles were successfully synthesized. In the FT-IR spectrum of the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (**Fig. 3.2c**), the absorption peaks at 3434 cm^{-1} and 1390 cm^{-1} were attributed to the C=N stretching vibration, indicating that the MIP was successfully formed. The characteristic peaks present in the spectra of ZnO@CF and Fe_3O_4-SiO_2-NH_2 were also present in the FT-IR spectrum of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

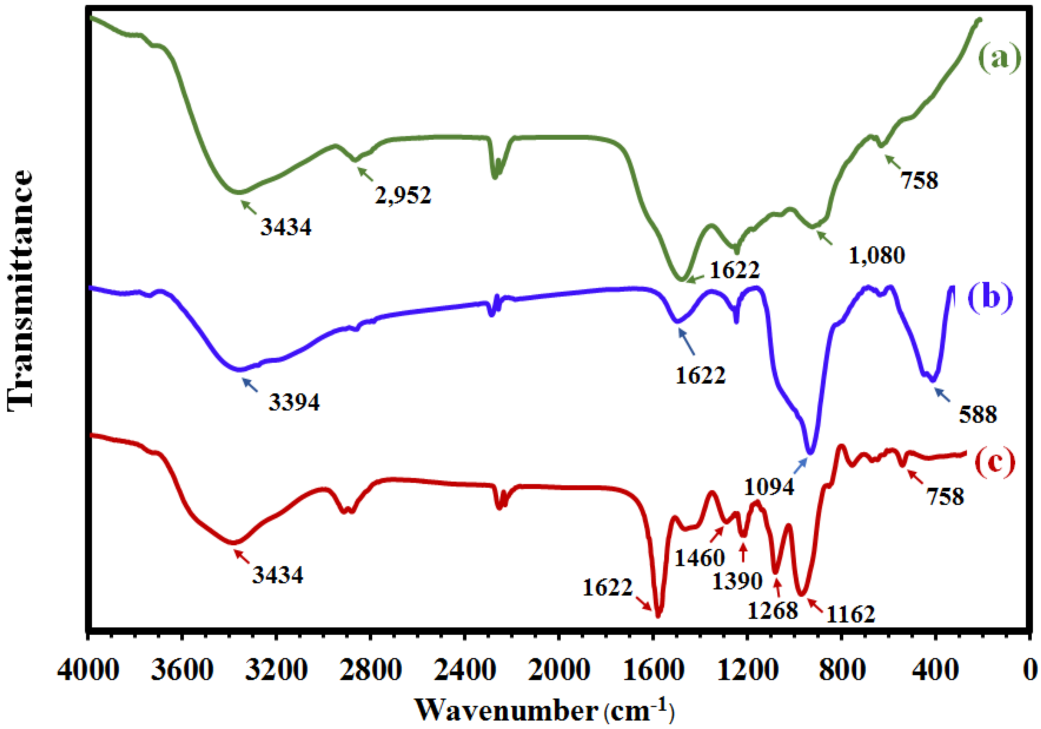


Fig. 3.2 FT-IR spectra of ZnO@CF (a), Fe_3O_4-SiO_2-NH_2 (b) and the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (c)

The FESEM images of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP and ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP adsorbents in **Fig. 3.3A** and **Fig. 3.3B** show that the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent has a rougher surface than the NIP adsorbent. The difference in the surface morphologies is due to the formation of specific recognition sites on the MIP adsorbent.

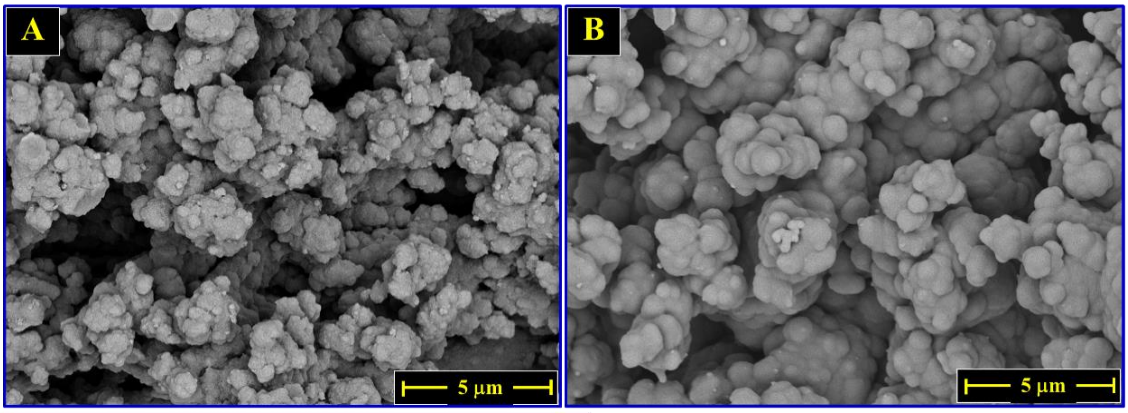


Fig. 3.3 FESEM images of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP (A) and ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP (B)

The magnetic properties of Fe_3O_4 and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent were measured by VSM technique. The saturation magnetizations of Fe_3O_4 nanoparticles and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP particles were 46.68 emu g^{-1} and 5.69 emu g^{-1}, respectively (**Fig. 3.4A**). Although the saturation magnetization of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP particles was lower than the saturation magnetization of the Fe_3O_4 nanoparticles, the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent could nevertheless be easily separated from the sample solution using a magnet (**Fig. 3.4B**).

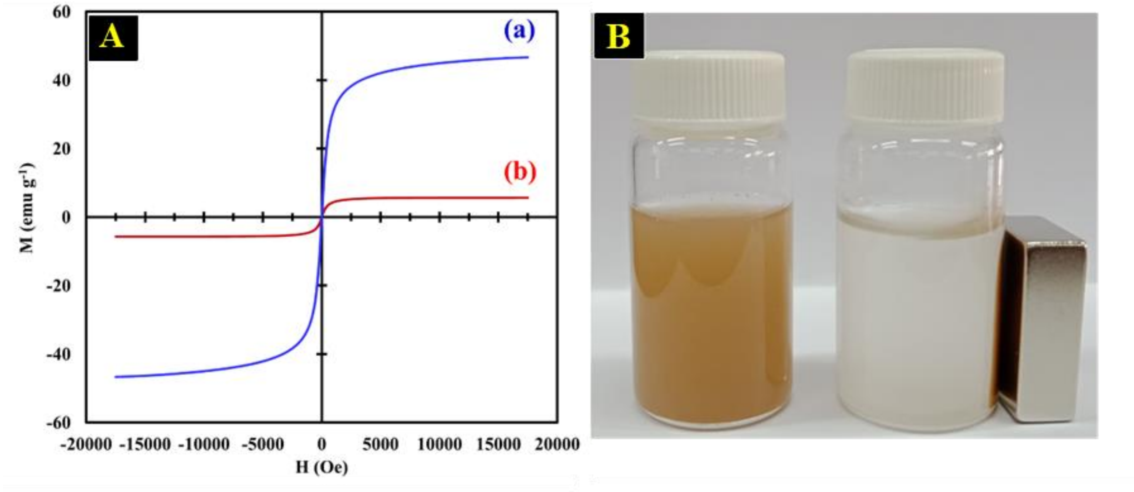


Fig. 3.4 VSM curves (A) of (a) Fe_3O_4 and (b) ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP; and Photograph of the dispersed composite adsorbent and the isolation of the adsorbent from sample solution (B)

The thermal stability of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was determined by TGA analysis. The adsorbent exhibited good stability in the range of 25–200 °C (**Fig. 3.5A**). The thermal stability of the nanocomposite is therefore more than adequate for d-MSPE at room temperature.

The XRD patterns of Fe_3O_4-SiO_2-NH_2 nanoparticles and the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent both present diffraction peaks at 2θ angles of 18°, 30°, 36°, 54°, 63° and 74° corresponding to (1 1 1), (2 2 0), (3 1 1), (4 2 2), (4 4 0), and (5 3 3) planes, respectively (**Fig. 3.5B**). These results are characteristic of crystalline cubic structures and demonstrated that the successful integration of ZnO@CF and Fe_3O_4-SiO_2-NH_2 with the MIP did not change their characteristics.

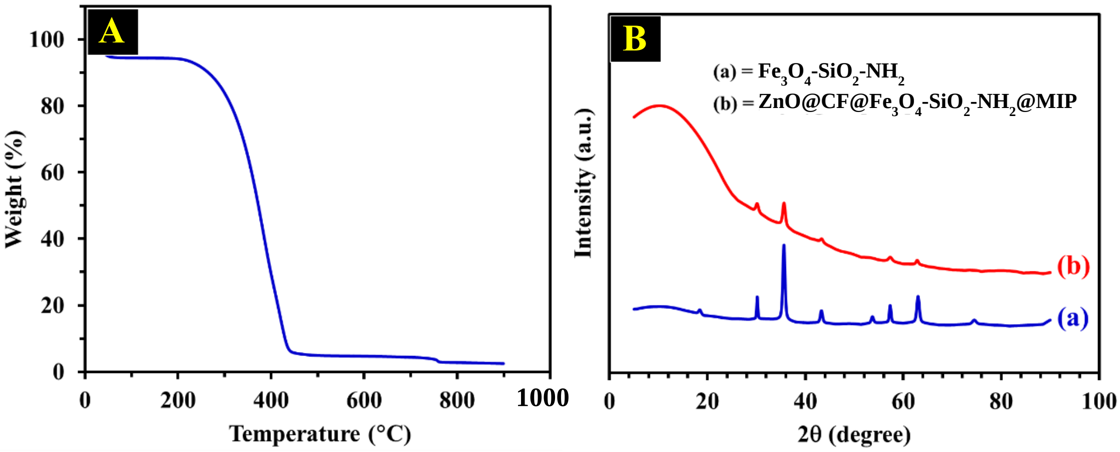


Fig. 3.5 TGA analysis curve (A) and XRD analysis (B) of Fe_3O_4-SiO_2-NH_2 and the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.3 Type of adsorbent

The extraction efficiency of different types of adsorbent were evaluated including Fe_3O_4-SiO_2-NH_2@NIP, ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP, Fe_3O_4-SiO_2-NH_2@MIP, and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbents (**Table 5 and Fig. 3.6**). The NIP adsorbents achieved lower extraction recoveries than the MIP adsorbents since, unlike the MIP adsorbents, they did not have specific recognition sites for sulfonamides. The ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP achieved higher recoveries than the Fe_3O_4-SiO_2-NH_2@MIP. The incorporated ZnO@CF nanocomposite improved the extraction efficiency of the adsorbent toward the target sulfonamides, and therefore the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was the most suitable of the present materials for the extraction of sulfonamides.

Table 5 The extraction recoveries of sulfonamides using different types of adsorbent

Adsorbent	Recovery (%) ± SD		
	SDZ	SMT	SDM
Fe_3O_4-SiO_2-NH_2@NIP	27.3±2.5	20.7±3.1	19.7±1.5
ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP	50.3±4.3	46.4±2.1	45.0±3.6
Fe_3O_4-SiO_2-NH_2@MIP	76.0±2.0	72.3±2.5	75.0±4.6
ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP	97.7±1.5	94.0±3.9	97.3±4.7

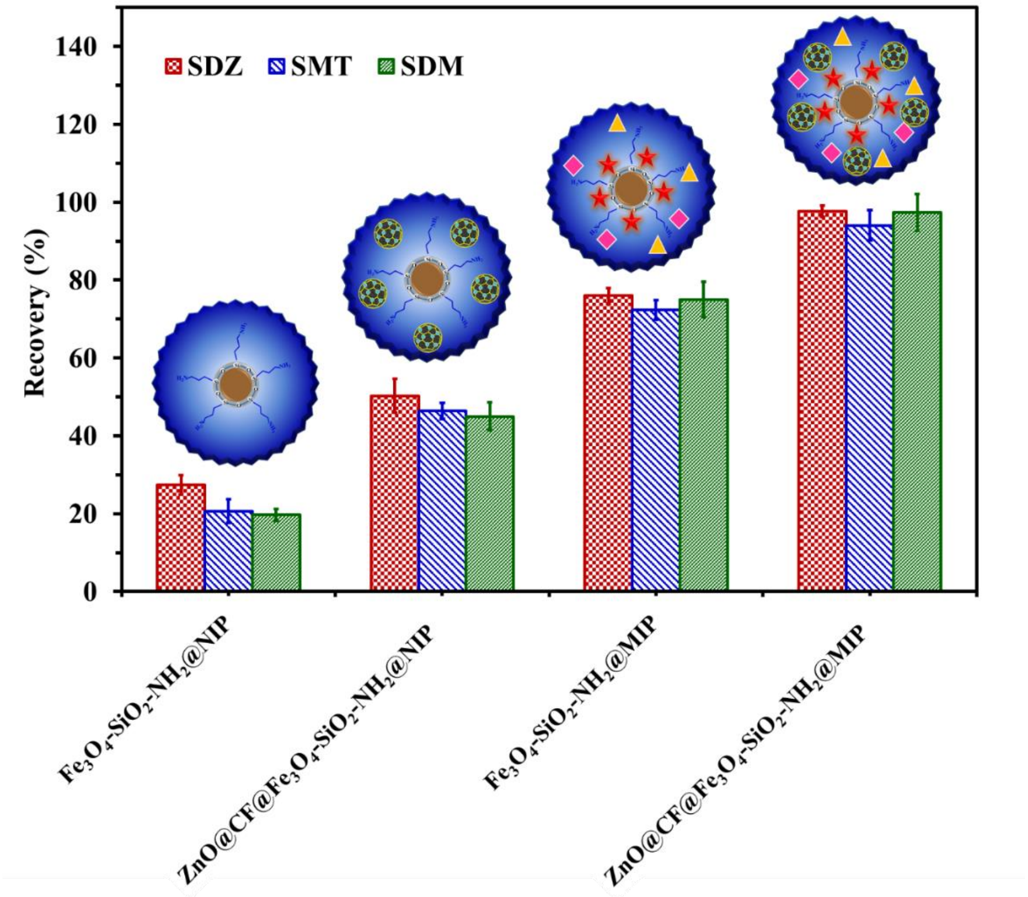


Fig. 3.6 Extraction efficiency of different adsorbents for the determination of sulfonamides

3.4 Optimization of adsorbent preparation and MSPE conditions

The extraction efficiency was considered in term of recovery as follows:

$$\text{Recovery (\%)} = (C_F V_F / C_I V_I) \times 100$$

Where C_F is the concentration of sulfonamides in the reconstituted solvent, C_I is the concentration of sulfonamides in spiked water sample. V_F and V_I are the volumes of the reconstituted solution (1.0 mL) and sample volume, respectively.

3.4.1 Effect of type of desorption solvent

Desorption of the three target sulfonamides from the nanocomposite adsorbent was performed with acetonitrile, ethyl acetate, acetone, methanol and a mixture of methanol and 2.0 % acetic acid. The mixture of methanol and 2.0 % acetic acid provided the best recovery (**Table 6 and Fig. 3.7**). The acidic condition can break hydrogen bonding and, therefore, may enable more complete desorption of sulfonamides from the nanocomposite adsorbent. At the same time, methanol can disrupt hydrophobic and π-π interactions. Therefore, methanol containing 2.0 % (v/v) acetic acid was the most effective desorption solvent investigated in this study.

Table 6 The extraction recoveries of sulfonamides using different types of desorption solvent

Types of desorption solvent	Recovery (%) ± SD		
	SDZ	SMT	SDM
Acetonitrile	54.3±4.0	51.7±1.5	58.3±1.8
Ethyl acetate	42.3±1.5	44.3±2.5	41.3±0.6
Acetone	32.0±2.8	33.9±3.1	26.9±4.4
Methanol	65.7±1.5	61.3±1.5	64.0±1.0
Methanol and 1% of acetic acid	76.7±1.5	76.0±1.7	76.0±1.0
Methanol and 2% of acetic acid	85.0±2.6	86.0±2.0	85.3±2.1

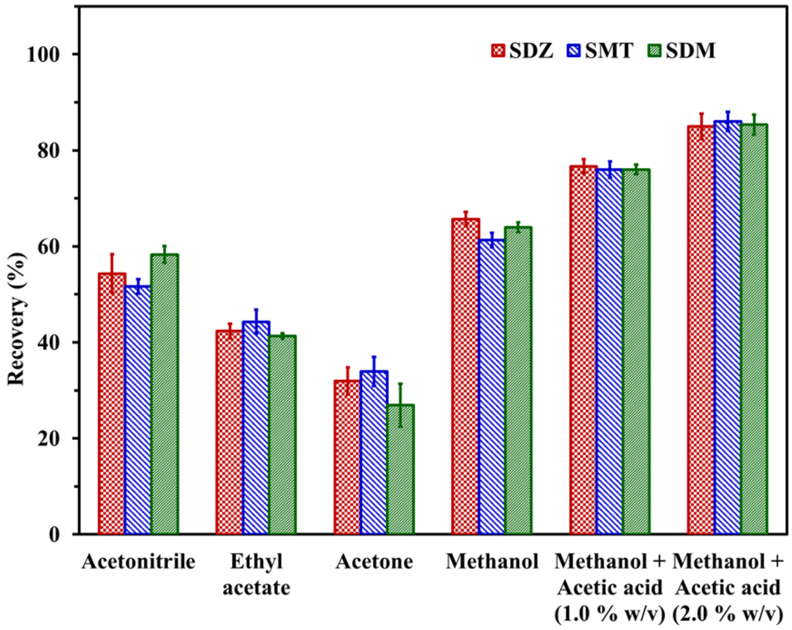


Fig. 3.7 Effect of the type of desorption solvent on the recovery of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.4.2 Effect of ionic strength of sample solution

The ionic strength of the aqueous sample solution can affect the adsorption of sulfonamides by reducing solubility. In this work, the effect of ionic strength was investigated by adding different concentrations of NaCl to the sample solution. The NaCl concentrations were 0.0, 1.0, 2.0, 5.0 and 10.0 % w/v. Extraction recoveries increased with increments of NaCl up to 5.0 % w/v and decreased at 10 %w/v (**Table 7 and Fig. 3.8**) since sodium and chloride ions can disturb the binding between sulfonamides and recognition sites of the adsorbent. Thus, 5.0 % w/v NaCl was dissolved in the sample solution before sulfonamides were extracted with the developed adsorbent.

Table 7 The extraction recoveries of sulfonamides using different amount of NaCl

Amount of NaCl (%w/v)	Recovery (%) ± SD		
	SDZ	SMT	SDM
0	41.4±3.7	42.5±3.6	50.2±5.5
1	63.3±3.5	66.3±1.5	74.7±2.5
2	77.7±1.5	79.7±2.1	81.0±2.6
5	90.3±2.3	92.7±2.5	96.0±2.6
10	77.7±1.5	78.3±1.5	81.7±1.5

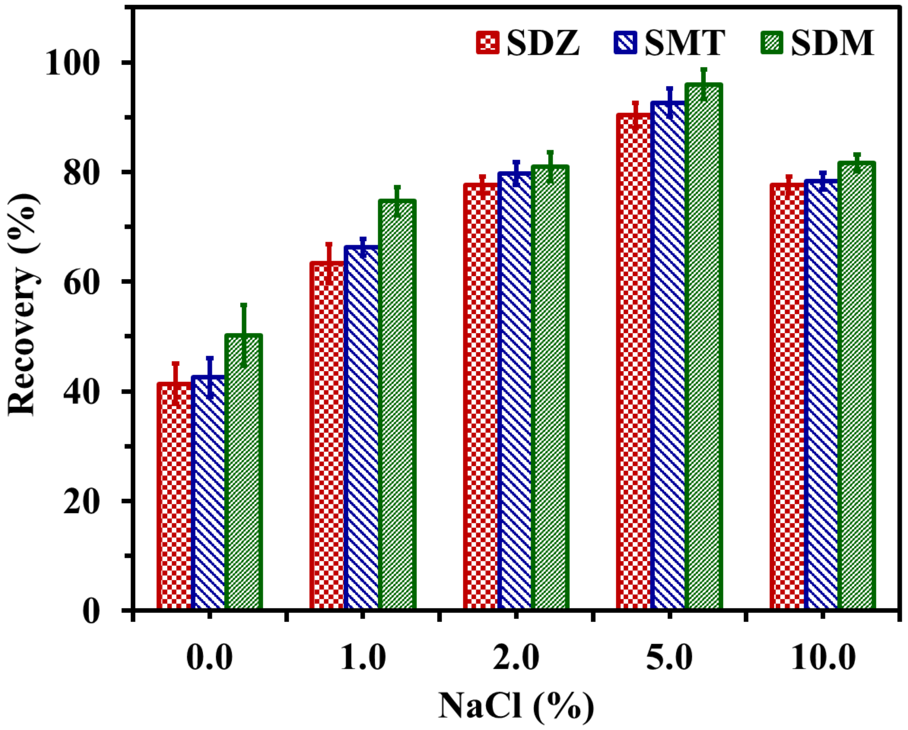


Fig. 3.8 Effect of ionic strength (NaCl) of sample solution on the extraction of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.4.3 Effect of desorption solvent volume

The effect of desorption solvent volume was also evaluated. The mixture of methanol and 2.0 % acetic acid was used at volumes of 1.0, 2.0, 4.0, and 6.0 mL. A volume of 2.0 mL was enough to desorb all target sulfonamides from the nanocomposite adsorbent (**Table 8 and Fig. 3.9**). Therefore, 2.0 mL of desorption solvent was selected for further experiments.

Table 8 The extraction recoveries of sulfonamides using different desorption volume

Desorption volume (mL)	Recovery (%) ± SD		
	SDZ	SMT	SDM
1	60.3±1.5	61.0±2.6	62.7±2.5
2	85.7±2.1	89.0±1.0	89.3±1.5
4	89.0±1.0	89.3±2.1	91.3±1.2
6	88.3±1.5	91.0±1.7	93.7±3.5

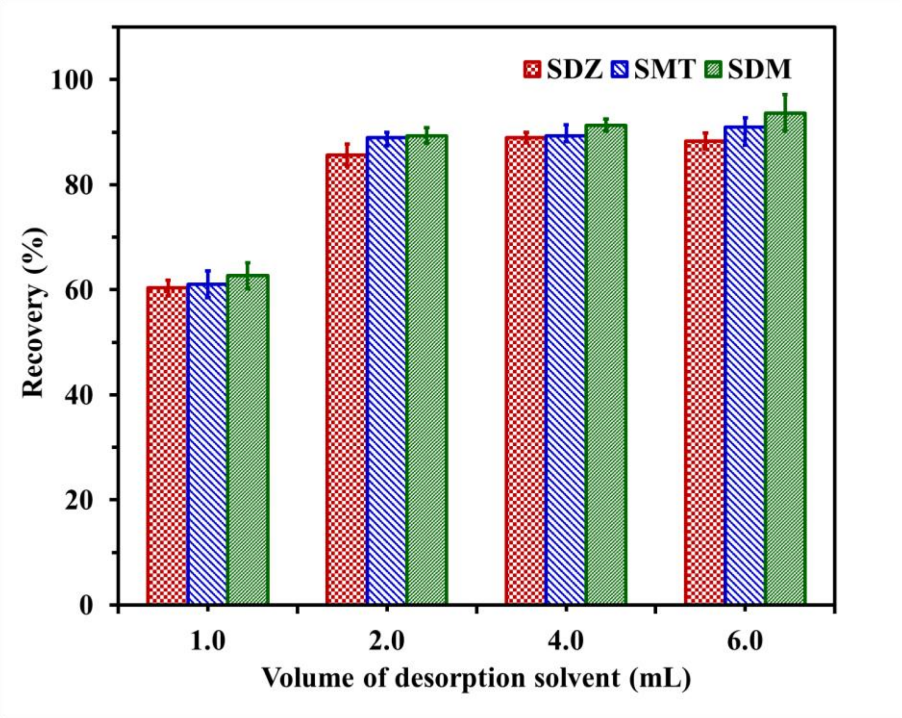


Fig. 3.9 Effect of desorption solvent volume on the desorption of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.4.4 Effect of desorption time

The desorption of sulfonamides from the nanocomposite adsorbent was performed under ultrasonication. Therefore, sonication duration was optimized. Desorption was evaluated at ultrasonication times of 10, 20, 30, and 40 min using 2.0 mL of a mixture of methanol and 2% acetic acid**.** The recovery increased with time and reached a maximum at 30 min (**Table 9 and Fig. 3.10**), which implied that all adsorbed sulfonamides were completely desorbed from the hierarchical nanocomposite adsorbent. Thus, sonication was performed for 30 min to desorb the target sulfonamides from the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

Table 9 The extraction recoveries of sulfonamides using different desorption time

Desorption time (min)	Recovery (%) ± SD		
	SDZ	SMT	SDM
10	39.0±3.6	40.3±2.5	41.0±2.6
20	72.3±3.8	71.7±3.8	82.3±5.9
30	88.7±1.5	90.7±2.1	92.0±2.0
40	90.0±2.6	91.3±2.1	90.3±1.5

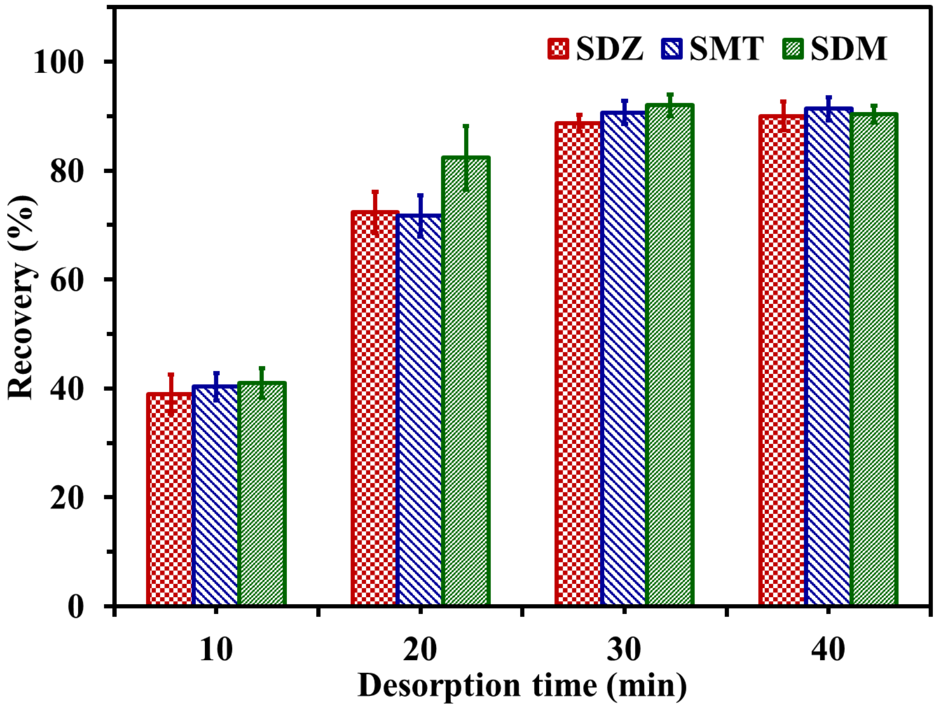


Fig. 3.10 Effect of sonication time on the desorption of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.4.5 Sample volume

The effect of the sample solution volume was investigated since it normally influences the extraction efficiency of target analytes and the enrichment factor. Large sample volumes produce high enrichment factors, however, too large a sample volume can reduce the extraction efficiency of the adsorbent. In this work, the effects of sample volumes ranging from 5 to 20 mL were evaluated. The recovery of sulfonamides decreased when sample volume exceeded 15 mL (**Table 10 and Fig. 3.11**) since the ratio of adsorbent to sample volume was too low. Considering the enrichment factor and extraction recovery of sulfonamides, a sample volume of 15 mL was chosen for further experiments.

Table 10 The extraction recoveries of sulfonamides using different sample volume

Sample volume (mL)	Recovery (%) ± SD		
	SDZ	SMT	SDM
5.0	86.7±1.5	88.7±1.5	89.3±0.6
10.0	86.3±1.5	87.0±1.0	87.7±0.6
15.0	85.6±3.0	89.3±0.6	88.0±1.7
20.0	68.7±1.5	68.7±1.5	67.7±3.1

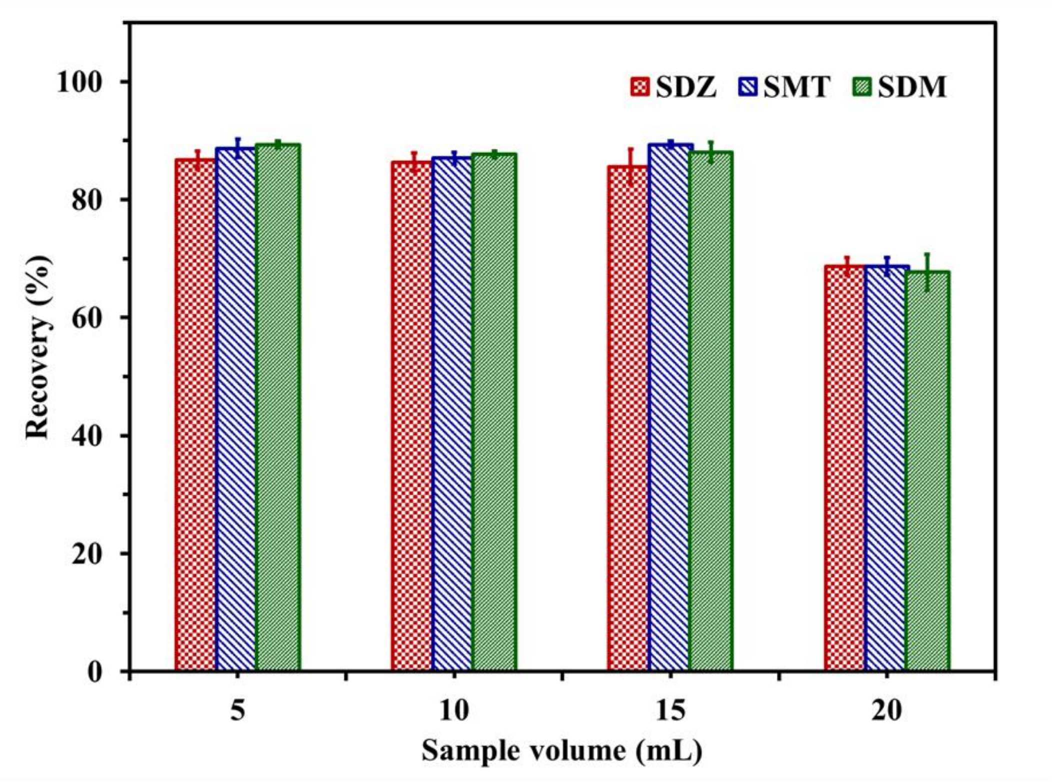


Fig. 3.11 Effect of sample volume on the extraction of sulfonamides using the hierarchical nanocomposite $ZnO@CF@Fe_3O_4\text{-}SiO_2\text{-}NH_2@MIP$ adsorbent

3.4.6 Effect of stirring rate of sample solution

The stirring rate of the sample solution typically affects the efficiency of d-MSPE. In this work, the stirring rate of the sample solution was varied from 500 to 1500 rpm. The extraction recovery was higher at 750 rpm than at 500 rpm and was lower at stirring rates above 750 rpm (**Table 11 and Fig. 3.12**). The reduced recovery at the higher stirring rates may be due to reduced contact between the adsorbent and target molecules. Moreover, higher stirring rates can damage adsorbents and affect reusability. Thus, the stirring rate of 750 rpm was selected for the adsorption of target sulfonamides with the nanocomposite $ZnO@CF@Fe_3O_4\text{-}SiO_2\text{-}NH_2@MIP$ adsorbent.

Table 11 The extraction recoveries of sulfonamides using different stirring rate

Stirring rate (rpm)	Recovery (%) ± SD		
	SDZ	SMT	SDM
500	81.3±1.5	82.3±2.1	81.7±2.1
750	88.7±1.5	89.3±3.2	87.3±2.9
1000	71.7±2.1	72.0±1.0	73.0±4.0
1250	63.7±3.2	62.0±3.6	66.0±3.0
1500	56.1±0.8	59.3±2.1	57.0±2.0

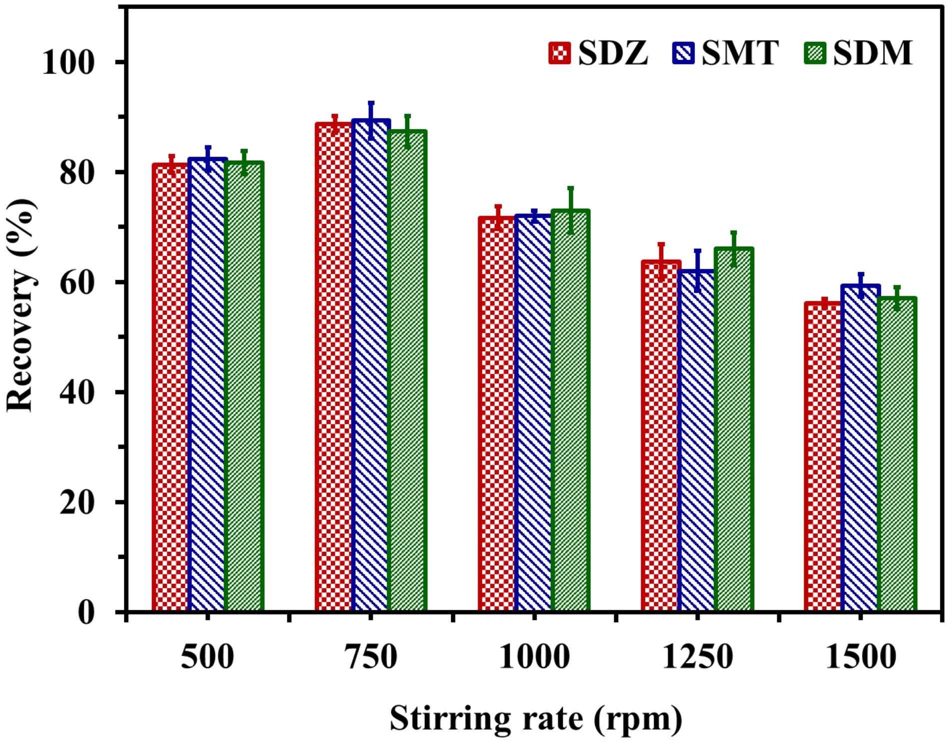


Fig. 3.12 Effect of stirring rate of sample solution on the adsorption of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2NH_2@MIP adsorbent

3.4.7 Effect of sample pH

The effect of sample pH is an important factor in the extraction process since the ionization and solubility of sulfonamides is affected by the pH of the sample solution. The sample pH was varied from 4 to 8 and the results are shown in **Table 12 and Fig. 3.13**. Recoveries were low at pH 4 and was not significantly different from pH 5 to pH 8. The low recovery at pH 4 may be due to the disruption of analyte-adsorbent binding by hydrogen ions in the elevated acidic condition. However, in this work, the pH of milk and water samples were between 5 and 8, and therefore sample pH adjustment was not required.

Table 12 The extraction recoveries of sulfonamides using different sample pH

Sample pH	Recovery (%) ± SD		
	SDZ	SMT	SDM
4	63.3±3.5	64.0±3.6	65.7±1.2
5	86.0±1.0	87.7±0.6	88.3±1.2
6	86.3±1.5	87.3±1.5	89.0±1.0
7	86.7±1.1	86.7±2.1	88.7±1.5
8	84.7±1.1	85.3±1.5	88.0±2.0

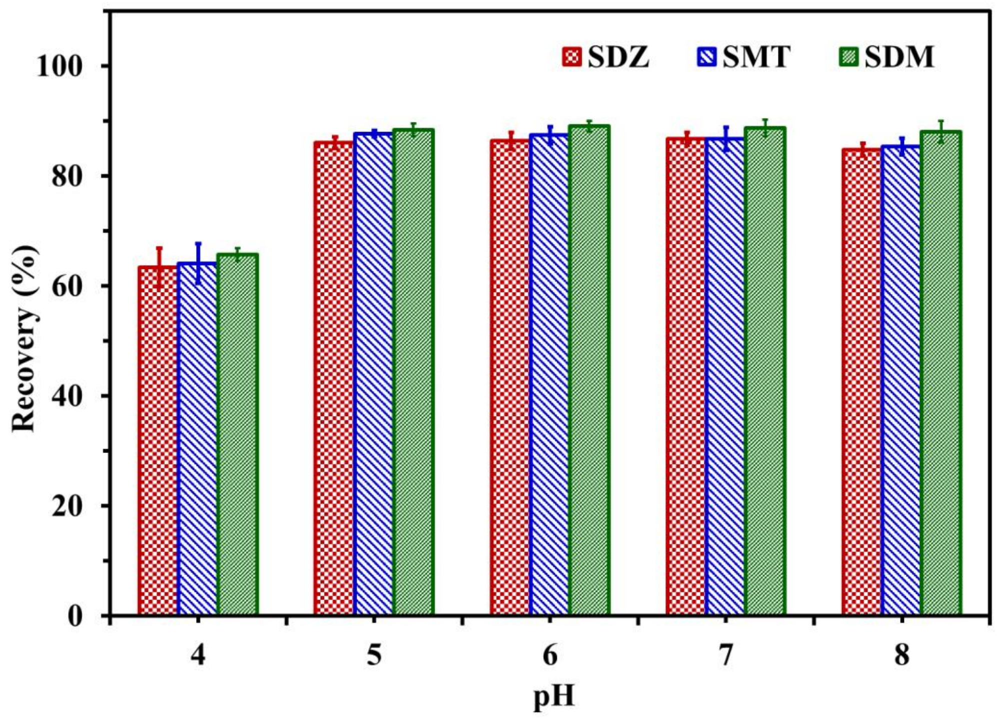


Fig. 3.13 Effect of sample pH on the extraction efficiency of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

3.4.8 Effect of extraction time

Since the contact time between adsorbent and analytes is an important factor in the d-MSPE, the effect of contact time between the sulfonamides and the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was investigated. Contact time was varied from 10 to 60 min. The extraction recovery increased from 10 to 30 min and extraction recovery remained almost constant at longer extraction times (**Table 13 and Fig. 3.14**). Thus, the extraction of sulfonamides with the developed adsorbent was performed for 30 min.

Table 13 The extraction recoveries of sulfonamides using different extraction time

Extraction time (min)	Recovery (%) ± SD		
	SDZ	SMT	SDM
10	34.4±5.9	34.3±5.8	37.0±5.2
20	61.0±4.6	58.7±2.3	59.3±3.1
30	89.0±1.0	89.7±2.5	90.3±3.2
40	88.3±2.1	91.0±4.6	90.7±2.1
60	84.7±0.6	86.0±2.0	86.7±2.1

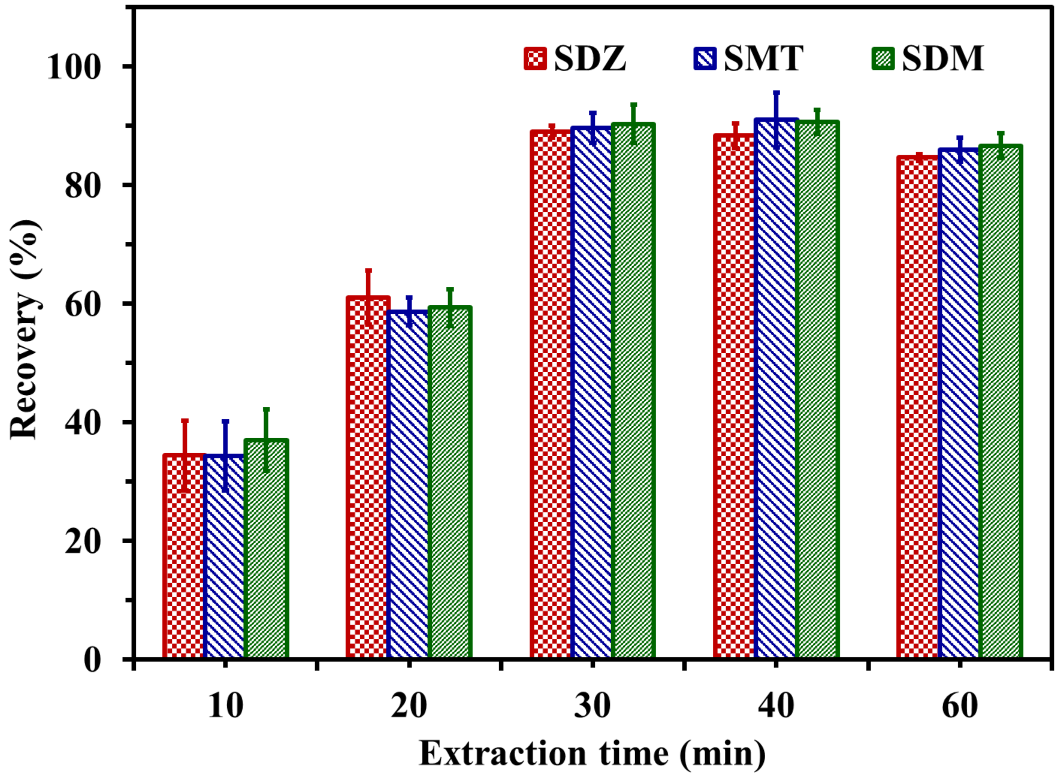


Fig. 3.14 Effect of extraction time on the recovery of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

The optimization of the d-MSPE using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the determination of sulfonamides are summarized in **Table 14**.

Table 14 The optimization of d-MSPE for the determination of sulfonamides

Parameters	Investigated values	Optimum condition
Type of adsorbent	Fe_3O_4-SiO_2-NH_2@NIP ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP Fe_3O_4-SiO_2-NH_2@MIP ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP	ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP
Type of desorption solvent	Acetonitrile, methanol, ethyl acetate, acetone, methanol and 1% of acetic acid methanol and 2% of acetic acid acetonitrile and 2% of acetic acid ethyl acetate and 1% of acetic acid ethyl acetate and 2% of acetic acid	Methanol and 2% of acetic acid
Salt addition (%w/v)	0.0, 1.0, 2.0, 5.0, 10.0	5.0
Desorption volume (mL)	1, 2, 4, 6	2
Desorption time (min)	10, 20, 30, 40	30
Sample volume (mL)	5, 10, 15, 20	15
Stirring rate (rpm)	500, 750, 1000, 1250, 1500	750
Amount of adsorbent (mg)	25, 50, 100, 150	50
Sample pH	No, 4, 5, 6, 7, 8	No effect
Extraction time (min)	10, 20, 30, 40, 60	30

3.5 Analytical Performances

The analytical performances of the developed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent coupled with HPLC-DAD were evaluated including linearity, LOD, LOQ, enrichment factor (EF) and repeatability.

3.5.1 Linearity, limit of detection (LOD) and limit of quantification (LOQ)

For the quantitative analysis, the linearity of an analytical method is vital. It is defined as the method's ability to produce results that are proportional to the concentrations of the analytes in the sample. The linearity was investigated using standard solutions of sulfadiazine, sulfamethazine and sulfadimethoxine in the concentration ranged of 2.0 to 150 µg L^{-1} (Each concentration was performed in triplicate). The linearity was plotted between the peak area versus the concentration of analytes and it is achieved the coefficient of determination (R^2) is equal or greater than 0.99 which was shown in **Table 15**.

Limit of detection (LOD) is the lowest amount of analyte in a sample that can be reliably detected and identified. LOD can be determined based on the signal-to-noise ratio. It is calculated by comparing the signal from sample measurement with a known low concentration of analyte and blank sample. Then, the minimum concentration is established. Usually, a signal-to-noise ratio of 3:1 or $S/N \geq 3$ is accepted (ICH, 1999). The LOD of the developed method was 2.0 µg L^{-1} as showed in **Table 15.**

Limit of quantitation (LOQ) can be defined as the lowest amount of analyte that can be determined. The determination should be done quantitatively with acceptable precision and accuracy. LOQ can be calculated based on signal-to-noise ratio. It is calculated by comparing the signal of sample with very low and know concentration of analyte with the blank samples. Then, it can be established which one analyte that is reliable. The signal-to-noise ratio of 10:1 or $S/N \geq 10$ is accepted (ICH, 1999). The LOQ of the developed method was 5.0 µg L^{-1} as showed in **Table 15**.

Table 15 The analytical performances for the extraction and determination of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

Analytes	Linear range	Calibration curve	R^2	LOD (µg L^{-1})	LOQ (µg L^{-1})
SDZ	2.0-150	y = 0.0440x-0.0006	0.9975	2.0	5.0
SMT	2.0-150	y = 0.0646x-0.0440	0.9996	2.0	5.0
SDM	2.0-150	y = 0.0867x-0.0721	0.9987	2.0	5.0

3.5.2 Enrichment factor (EF) and repeatability

Enrichment factors were calculated from the ratio of the concentration of each sulfonamide after extraction to the initial concentration of the sample solution (EF = C_{MSPE}/C_0). The enrichment factor for sulfadiazine, sulfamethazine and sulfadimethoxine were 12.6, 12.8 and 13.9, respectively. The evaluation of the repeatability was based on intra-day and inter-day precision. The RSD of intra-day and inter-day precisions were investigated within one day and six different days. These results indicated outstanding repeatability of the developed approach. The results are presented in **Table 16**.

Table 16 The enrichment factor (EF) and repeatability for the extraction and determination of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

Analytes	Enrichment factor	Repeatability	
		Intra-day (n=6) (RSD %)	Inter-day (n=6) (RSD %)
SDZ	12.6	4.0	5.4
SMT	12.8	3.4	5.0
SDM	13.9	4.4	5.4

3.5.3 Reusability

The reusability of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was investigated by repeated the extraction of sulfonamides in milk. To eliminate any carry-over effect, the used adsorbent was cleaned before the next extraction by washing with 2.0 mL methanol and DI water, respectively. The developed adsorbent can be reused up to 5 times before the recovery of sulfonamides falls below 80 % (**Table 17 and Fig. 3.15**). The decreasing of extraction recovery after 5 extraction cycles may be due to the loss of adsorption material during the washing step and the possible adsorption through non-specific interaction of some interferences. The developed composite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction of sulfonamides in real samples can be effectively used for 5 adsorption-desorption cycles.

Table 17 The extraction recoveries of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

Extraction cycles	Recovery (%) ± SD		
	SDZ	SMT	SDM
1	86.3±1.5	89.7±0.6	89.0±1.0
2	86.3±1.5	89.7±3.8	90.7±3.8
3	86.7±3.1	88.0±2.6	89.3±2.5
4	88.0±5.6	89.0±3.0	89.0±5.6
5	86.0±2.0	86.0±1.7	85.3±2.1
6	76.3±2.5	74.0±3.6	74.3±3.1

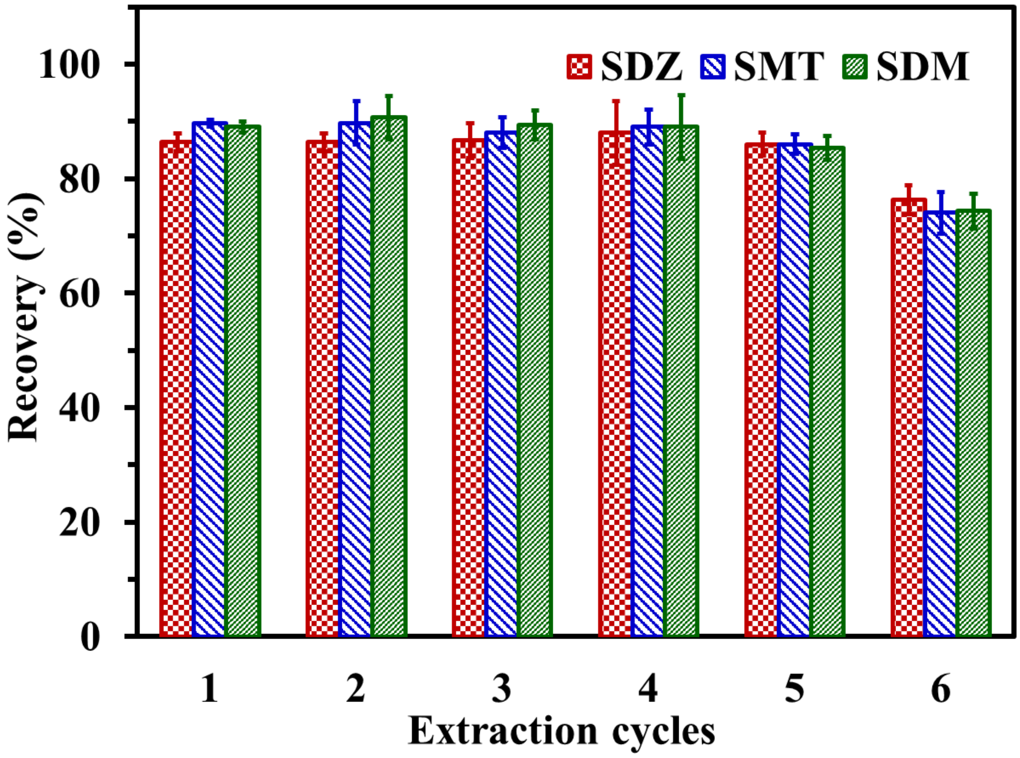


Fig. 3.15 The reusability of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction and determination of sulfonamides

3.5.4 Comparison with C18 sorbent

The extraction efficiency of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent toward the target sulfonamides was compared with the efficiency of a commercial C18 SPE sorbent. The developed adsorbent achieved recoveries from 91.6 to 96.0 % and the C18 adsorbent achieved recoveries from 85.7 to 88.0% (**Fig. 3.16**). The developed adsorbent performs well and has excellent selectivity. It is also simple, convenient and rapid to use. The developed adsorbent can be applied to determine sulfonamides in complex samples.

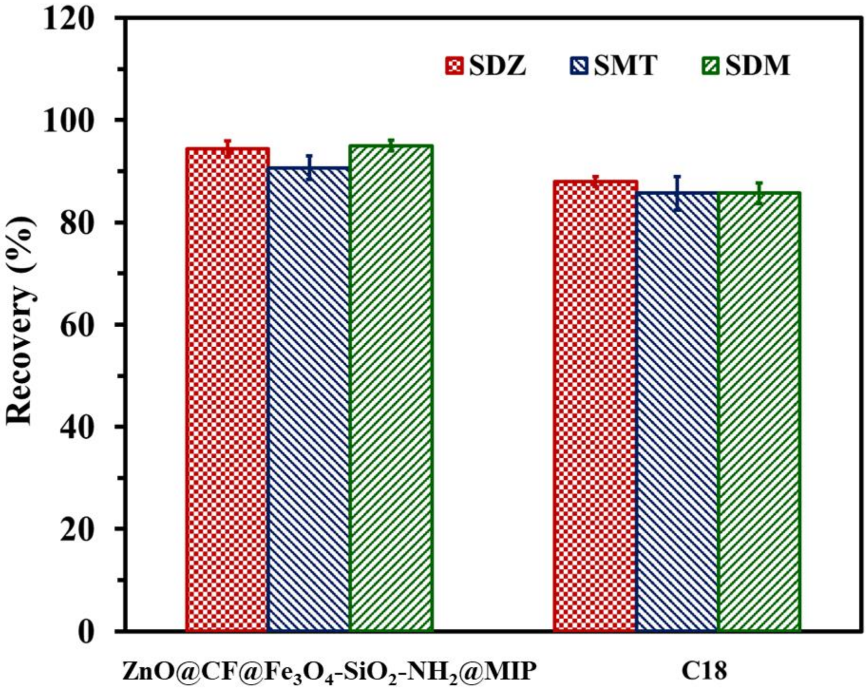


Fig. 3.16 Recoveries of sulfonamides using the hierarchical nanocomposite $ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP$ and a C18 adsorbent

3.5.5 Analysis of sulfonamides in milk and water samples

The developed hierarchical nanocomposite $ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP$ adsorbent was applied to extract and determine sulfonamides in milk and aquaculture water samples. Concentrations of sulfadiazine found in some samples lower than the maximum residue limits (**Table 18**). The accuracy was also determined by spiking standard sulfonamides in real samples at 10, 20 and 50 μg L^{-1}. The accuracy was evaluated in terms of relative recovery, which was calculated according to the following equation:

Relative recovery (%) = $(C_T-C_S)/C_{Spike}$ *100, where C_T is the total sulfonamides in the sample after spiking with the standard, C_S is the concentration of residual sulfonamides in the sample, and C_{Spike} is the concentration of sulfonamides spiked in the sample. The relative recoveries from the milk samples ranged from 84.3 to 96.2 % and water samples from 85.4 to 96.0 %. The RSDs ranged from 2.4 to 6.2%. The HPLC chromatograms for a milk sample, standard sulfonamides, and a spiked milk sample are shown in **Fig. 3.17**.

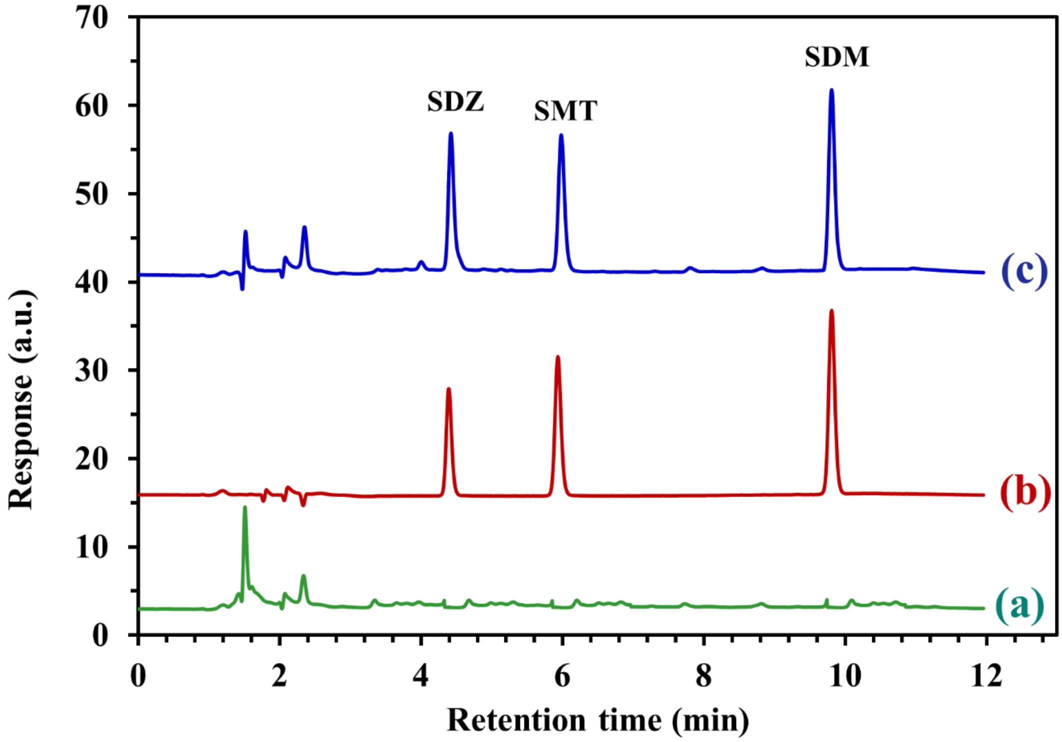


Fig. 3.17 Chromatograms show sulfonamides extracted from a real milk sample (a), standard sulfonamides solution (b), and a spiked milk sample (c)

Table 18 The determination of sulfonamides in milk and water samples using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent coupled with HPLC-DAD

Sample	Added (μg kg^{-1})	SDZ			SMT			SDM		
		F (μg L^{-1})	RR (%)	RSD (%)	F (μg L^{-1})	RR (%)	RSD (%)	F (μg L^{-1})	RR (%)	RSD (%)
Milk 1	0.00	-	-	-	-	-	-	-	-	-
	10.0	8.43	84.3	5.9	8.55	85.5	5.1	9.26	92.6	5.3
	20.0	18.12	91.0	4.8	17.21	86.0	4.8	18.90	94.5	5.1
	50.0	46.90	93.8	2.9	42.89	85.8	3.9	48.10	96.2	2.9
Milk 2	0.00	-	-	-	-	-	-	-	-	-
	10.0	8.44	84.4	4.8	9.30	93.0	5.9	9.01	90.1	4.0
	20.0	18.39	91.9	3.9	17.42	87.1	4.6	18.45	92.3	3.8
	50.0	45.20	90.4	2.4	43.98	88.0	3.0	46.10	92.2	1.8
Milk 3	0.00	2.50	-	5.0	-	-	-	-	-	-
	10.0	11.89	93.9	4.8	9.03	90.3	5.6	8.67	86.7	5.0
	20.0	21.09	93.0	4.5	18.90	94.5	4.8	17.90	89.5	4.3
	50.0	49.80	94.6	4.0	46.09	92.2	4.6	45.98	92.0	2.6
Water 1	0.00	2.05	-	4.0	-	-	-	-	-	-
	10.0	11.05	90.0	3.8	8.67	86.7	4.0	8.90	89.0	4.2
	20.0	20.10	90.2	3.5	17.87	89.4	3.7	18.08	90.4	2.6
	50.0	50.05	96.0	3.5	46.80	93.6	3.8	47.0	94.0	3.0
Water 2	0.00	-	-	-	-	-	-	-	-	-
	10.0	8.69	86.9	6.0	8.65	86.5	5.9	8.90	89.0	6.2
	20.0	18.21	91.1	4.8	19.03	95.1	4.5	17.43	87.1	3.9
	50.0	45.90	91.8	3.0	45.89	91.8	4.0	45.00	90.0	4.0
Water 3	0.00	-	-	-	-	-	-	-	-	-
	10.0	8.78	87.8	5.8	8.56	85.6	4.6	8.68	86.8	5.6
	20.0	17.89	89.4	4.8	17.08	85.4	4.2	18.08	90.4	3.8
	50.0	45.60	91.2	4.5	45.89	91.8	4.3	47.05	94.1	3.6

3.5.6 Comparison with other works

The analytical performances of the developed method were compared with those of other methods previously reported for the extraction and determination of sulfonamides. The comparison is summarized in **Table 19**. The developed method provided comparable or better extraction recoveries than other methods. The LOD of the developed method is also comparable with other methods. In addition, the developed nanocomposite adsorbent is highly specific for sulfonamides which enables its application in a variety of matrix samples. Thus, the developed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent presents a highly effective and selective alternative method of extracting sulfonamides, which is also simple, rapid and convenient to perform.

Table 19 The analytical method for the determination of sulfonamides in various samples

Extraction method	Method	Extractant	Sample	Sample amount	Elution volume (mL)	LOD (µg L^{-1})	Recovery (%)	References
MSPE	HPLC-DAD	Fe_3O_4–GOx	Water	1 mL	1	0.05-0.10	67.4-119.9	(P. Shi & Ye, 2014)
MSPE	HPLC-UV	$CoFe_2O_4$-graphene	Milk	1.5 mL	0.5	1.16-1.59	62.0-104.3	(Y. Li et al., 2015)
MSPE	HPLC-UV	MIP-pGMA@A-MNPs	Feed	7 g	2	16	89.3-107.0	(Feng et al., 2016)
SLE	HPLC-DAD	MeOH and ACN	Shrimp	1 g	0.5	8.4-10.9	81.6-116.8	(Charitonos et al., 2017)
SPE	HPLC-DAD	Sol-gel/MIP	Milk	1 g	2	1.9-13.3	85.8-109.2	(Kechagia et al., 2018)
SPE	HPLC-UV	MIP	Soil	10 mL	1	1.0	95.0-105.0	(Zhu et al., 2019)
SPE	HPLC-DAD	VTTS-MGO@mSiO_2/MIP	Water	50 mL	2	0.010-0.014	87.4-102.3	(Fan et al., 2020)
d-MSPE	HPLC-UV	YS-Fe_3O_4@GC	Milk	25 mL	1.8	0.11-0.25	77.2-118.0	(Liu et al., 2020)
MSPE-i- DLLME	HPLC-DAD	MCNs	Food stuffs	100 mL	1	0.01-5	70.0-90.0	(Yazdanfar et al., 2021)
MSPE	HPLC-DAD	ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP	Milk and water	15 mL	2	2.0	84.3-96.2	This work

MSPE = magnetic solid phase extraction, SLE = solid liquid extraction, SPE = solid phase extraction, d-MSPE = dispersive magnetic solid phase extraction, DLLME = liquid liquid micro-extraction: DAD = diode array detection, UV = ultra-violet detection, Fe_3O_4–GOx = Fe_3O_4–graphene oxide, $CoFe_2O_4$-graphene = graphene-based magnetic nanocomposite, MIP = molecularly imprinted polymer, pGMA =poly(glycidyl methacrylate), A-MNPs = amino-functionalized magnetic nanoparticles, MGO@mSiO_2 = magnetic graphene oxide, VTTS-MGO@mSiO_2 = magnetic graphene oxide modified with vinyl groups, LPME = liquid phase microextraction, YS-Fe_3O_4@GC = yolk-shell Fe_3O_4@graphitic carbon, MCNs = magnetic carbon nanocomposite

3.5.7 Adsorption kinetics

Pseudo-first order (PFO) and pseudo-second order (PSO) models were used to investigate the adsorption kinetics between the developed hierarchical nanocomposite $ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP$ adsorbent and the target sulfonamides. The PFO model describes the adsorption of sulfonamides onto the nanocomposite adsorbent according to the following equation:

$$\log(q_e - q_t) = \log q_e - \frac{k_1}{2.303} t$$

By plotting log ($q_e - q_t$) versus t, the first-order rate constant k_1 and the equilibrium capacity (q_e) can be estimated from the slope and intercept, respectively.

The PSO model is based on the amount of sulfonamides on the nanocomposite adsorbent according to following equation:

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

where q_t (mg g^{-1}) is the amount of adsorbed analyte at a given time and q_e (mg g^{-1}) is the equilibrium adsorption capacity. By plotting t/qt versus t, the second-order rate constant (k_2) and the equilibrium capacity (q_e) are obtained from the intercept and slope, respectively.

It can be seen that the coefficient of determination ($R^2 > 0.999$) of fitting with the PSO model are better than the R^2 values of fitting with the PFO model (**Table 20**). These results confirmed that the adsorption kinetics are governed by chemisorption.

Table 20 The linear regression of the pseudo-first order and pseudo-second order models for the adsorption of three target sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

Analyte	Coefficient of determination (R^2)	
	Pseudo-first order	Pseudo-second order
SDZ	0.0393	0.9999
SMT	0.0100	0.9991
SDM	0.0079	0.9992

4. Concluding remark

A novel hierarchical nanocomposite adsorbent was successfully designed and fabricated using zinc oxide, carbon foam, silica-coated magnetite nanoparticles, and molecularly imprinted polymer. The fabricated adsorbent was used for the extraction and determination of sulfonamides. The nanocomposite of zinc oxide and carbon foam exhibited a high adsorption ability, the molecularly imprinted polymer was highly specific toward the target molecules, and the magnetite nanoparticles enabled simple isolation of the adsorbent. The developed method achieved good recoveries (84.3-96.2%) of sulfonamides and exhibited good selectivity and repeatability. The nanocomposite adsorbent is simple to fabricate, convenient to use, rapid, and its stability allows reuse. The developed approach can be modified and applied to extract and determine other compounds in various sample matrices.

References

1. Ayankojo, A. G., Reut, J., Opik, A., & Syritski, V. Sulfamethizole-imprinted polymer on screen-printed electrodes: Towards the design of a portable environmental sensor. Sensors and Actuators B-Chemical, 320 (2020) 9.
2. Bogdanova, A. Pochivalov, C. Vakh, A. Bulatov, Supramolecular solvents formation in aqueous solutions containing primary amine and monoterpenoid compound: Liquid phase microextraction of sulfonamides. Talanta, 216 (2020) 120992.
3. Charitonos, S., Samanidou, V. F., & Papadoyannis, I. Development of an HPLC-DAD Method for the Determination of Five Sulfonamides in Shrimps and Validation According to the European Decision 657/2002/EC. Food Analytical Methods, 10 (2017) 2011-2017.
4. Chatzimitakos, C. Stalikas, Zinc ferrite as a magnetic sorbent for the dispersive micro solid-phase extraction of sulfonamides and their determination by HPLC. Microchemical Journal, 155 (2020) 104670.
5. Cheng, J. Zhao, X. Wang, C. Yang, S. Li, T. Lu, X. Li, X. Wang, G. Zhu, A highly sensitive and selective method for the determination of ceftiofur sodium in milk and animal-origin food based on molecularly imprinted solid-phase extraction coupled with HPLC-UV. Food Chemistry, 347 (2021) 129013.
6. Di, X. Wang, Y. Liu, X. Guo, X. Di, Microwave assisted extraction in combination with solid phase purification and switchable hydrophilicity solvent-based homogeneous liquid-liquid microextraction for the determination of sulfonamides in chicken meat. Journal of Chromatography B, 1118-1119 (2019) 109-115.
7. Du, B. Zhang, P. Guo, G. Chen, C. Chang, Q. Fu, Facile preparation of magnetic molecularly imprinted polymers for the selective extraction and determination of dexamethasone in skincare cosmetics using HPLC. Journal of Separation Science, 41 (2018) 2441-2452.
8. Fan, G.L. Zeng, X.G. Ma, Effects of prepolymerization on surface molecularly imprinted polymer for rapid separation and analysis of sulfonamides in water. Journal of Colloid and Interface Science, 571 (2020) 21-29.

9. Feng, H.Y. Li, L. Zhang, J.Y. Zhang, J.P. Dai, X.J. Wang, L.L. Zhang, Y.J. Wei, Preparation and application of novel magnetic molecularly imprinted composites for recognition of sulfadimethoxine in feed samples. Analytical Sciences, 32 (2016) 517-521.

10. Gao, Y.T. Guo, X.Y. Li, X.D. Wang, J.X. Wang, F.Y. Qian, H.D. Gu, Z.N. Zhang, Magnetic solid phase extraction of sulfonamides based on carboxylated magnetic graphene oxide nanoparticles in environmental waters. Journal of Chromatography A, 1575 (2018) 1-10.

11. Herrero-Latorre, J. Barciela-García, S. García-Martín, R.M. Peña-Crecente, J. Otárola-Jiménez, Magnetic solid-phase extraction using carbon nanotubes as sorbents: A review. Analytica Chimica Acta, 892 (2015) 10-26.

12. Jalilian, H. Ebrahimzadeh, A.A. Asgharinezhad, P. Khodayari, Magnetic molecularly imprinted polymer for the selective dispersive micro solid phase extraction of phenolphthalein in urine samples and herbal slimming capsules prior to HPLC-PDA analysis. Microchemical Journal, 160 (2021) 105712.

13. Ji, Y.Y. Shi, L. Wang, J.H. Lu, C. Ferronato, J.M. Chovelon, Sulfate radical-based oxidation of antibiotics sulfamethazine, sulfapyridine, sulfadiazine, sulfadimethoxine, and sulfachloropyridazine: Formation of SO_2 extrusion products and effects of natural organic matter. Science of the Total Environment, 593 (2017) 704-712.

14. Jia, P. Zhao, X. Ye, L. Zhang, T. Wang, Q. Chen, X. Hou, A novel metal-organic framework composite MIL-101(Cr)@GO as an efficient sorbent in dispersive micro-solid phase extraction coupling with UHPLC-MS/MS for the determination of sulfonamides in milk samples. Talanta, 169 (2017) 227-238.

15. Jullakan, S., & Bunkoed, O. A nanocomposite adsorbent of metallic copper, polypyrrole, halloysite nanotubes and magnetite nanoparticles for the extraction and enrichment of sulfonamides in milk. Journal of Chromatography B, 1180 (2021) 122900.

16. Kester, K.D. Karpa, K.E. Vrana, 4 - Treatment of Infectious Diseases, in: M. Kester, K.D. Karpa, K.E. Vrana (Eds.) Elsevier's integrated review pharmacology (Second Edition). W.B. Saunders, Philadelphia, (2012) 41-78.

17. Li Juan, Y., Ci Dan, Z. X., Liao, Q. G., Da Wen, Z., & Lin Guang, L. Pipette-tip solid-phase extraction using cetyltrimethylammonium bromide enhanced molybdenum disulfide nanosheets as an efficient adsorbent for the extraction of sulfonamides in environmental water samples. Journal of Separation Science, 43 (2020) 905-911.
18. Li & He, B. Ultrasensitive sandwich-type electrochemical biosensor based on octahedral gold nanoparticles modified poly (ethylenimine) functionalized graphitic carbon nitride nanosheets for the determination of sulfamethazine. Sensors and Actuators B-Chemical, 329 (2021) 129158.
19. Li, N. Zhu, T. Chen, Y. Ma, Q. Li, A green cyclodextrin metal-organic framework as solid-phase extraction medium for enrichment of sulfonamides before their HPLC determination. Microchemical Journal, 138 (2018) 401-407.
20. Liang, Y. Lu, N. Li, H. Li, F. Zhu, Microwave-assisted synthesis of magnetic surface molecular imprinted polymer for adsorption and solid phase extraction of 4-nitrophenol in wastewater. Microchemical Journal, 159 (2020) 105316.
21. Lin, L. Li, G.Y. Fu, Z.Z. Lai, A.H. Peng, Z.Y. Huang, Molecularly imprinted polymer-based photonic crystal sensor array for the discrimination of sulfonamides. Analytica Chimica Acta, 1101 (2020) 32-40.
22. Liu, X., Tong, Y., & Zhang, L. Tailorable yolk-shell Fe_3O_4@graphitic carbon submicroboxes as efficient extraction materials for highly sensitive determination of trace sulfonamides in food samples. Food Chemistry, 303 (2020) 125369.
23. Lu, C. Liu, M. Qin, J. Deng, G. Shi, T. Zhou, Functionalized ionic liquids-supported metal organic frameworks for dispersive solid phase extraction of sulfonamide antibiotics in water samples. Analytica Chimica Acta, 1133 (2020) 88-98.
24. Lu, D., Liu, C., Qin, M., Deng, J., Shi, G., & Zhou, T. Functionalized ionic liquids-supported metal organic frameworks for dispersive solid phase extraction of sulfonamide antibiotics in water samples. Analytica Chimica Acta, 1133 (2020) 88-98.
25. Moga, A., Vergara-Barberán, M., Lerma-García, M. J., Herrero-Martínez, J. M., & Simó-Alfonso, E. F. Poly(ethylene glycol) diacrylate-based solid-phase

extraction for determination of sulfonamides in meat samples. Microchemical Journal, 157 (2020) 104931.

26. Mohamed, P.Y. Khashaba, M.M. El-Wekil, R.Y. Shahin, Spectrodensitometric determination of rivastigmine after vortex assisted magnetic solid phase extraction. Microchemical Journal, 147 (2019) 764-774.
27. Mokhtar, R.A. Abdel-Salam, G.M. Hadad, Tolerance intervals modeling for design space of a salt assisted liquid-liquid microextraction of trimethoprim and six common sulfonamide antibiotics in environmental water samples. Journal of Chromatography A, 1586 (2019) 18-29.
28. Mukherjee, Chapter 13 - Bioassay-Guided Isolation and Evaluation of Herbal Drugs, in: P.K. Mukherjee (Ed.) Quality control and evaluation of herbal drugs. Elsevier, (2019) 515-537.
29. Nasir, N. Yahaya, N.N.M. Zain, V. Lim, S. Kamaruzaman, B. Saad, N. Nishiyama, N. Yoshida, Y. Hirota, Thiol-functionalized magnetic carbon nanotubes for magnetic micro-solid phase extraction of sulfonamide antibiotics from milks and commercial chicken meat products. Food Chemistry, 276 (2019) 458-466.
30. Rozaini, N.F. Semail, B. Saad, S. Kamaruzaman, W.N. Abdullah, N.A. Rahim, M. Miskam, S.H. Loh, N. Yahaya, Molecularly imprinted silica gel incorporated with agarose polymer matrix as mixed matrix membrane for separation and preconcentration of sulfonamide antibiotics in water samples. Talanta, 199 (2019) 522-531.
31. Sadeghi, 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 methodology. Microchemical Journal, 146 (2019) 974-985.
32. Salehi, S. Rasoul-Amini, N. Adib, M. Shekarchi, Synthesis of molecular imprinted polymers for selective extraction of domperidone from human serum using high performance liquid chromatography with fluorescence detection. Journal of Chromatography B, 1027 (2016) 165-173.

33. Shakirova, F., Shishov, A., & Bulatov, A. Automated liquid-liquid microextraction and determination of sulfonamides in urine samples based on Schiff bases formation in natural deep eutectic solvent media. Talanta, 234 (2021) 122660.

34. Shi, X. Z., Meng, Y., Liu, J. H., Sun, A. L., Li, D. X., Yao, C. X., et al. Group-selective molecularly imprinted polymer solid-phase extraction for the simultaneous determination of six sulfonamides in aquaculture products. Journal of Chromatography B, 879 (2011) 1071-1076.

35. Shishov, A., Gorbunov, A., Baranovskii, E., & Bulatov, A. Microextraction of sulfonamides from chicken meat samples in three-component deep eutectic solvent. Microchemical Journal, 158 (2020).

36. Su, S. Xia, R. Wang, L. Xiao, 13 - Phytohormonal quantification based on biological principles, in: J. Li, C. Li, S.M. Smith (Eds.) Hormone Metabolism and Signaling in Plants. Academic Press, (2017) 431-470.

37. Sukchuay, T., Kanatharana, P., Wannapob, R., Thavarungkul, P., & Bunkoed, O. Polypyrrole/silica/magnetite nanoparticles as a sorbent for the extraction of sulfonamides from water samples. Journal of Separation Science, 38 (2015), 3921-3927.

38. Tang, F. Wei, X. Wang, Y. Ma, Y. Song, Y. Ma, Q. Song, G. Xu, Y. Cen, Q. Hu, Determination of semicarbazide in fish by molecularly imprinted stir bar sorptive extraction coupled with high performance liquid chromatography. Journal of Chromatography B, 1076 (2018) 8-14.

39. Turiel, A.M. Esteban, 8 - Molecularly imprinted polymers, in: C.F. Poole (Ed.) Solid-Phase Extraction. Elsevier2020, pp. 215-233.

40. Wang, L. Zhang, Y.P. Song, J.X. Liu, J.P. Wang, Application of molecularly imprinted polymer based matrix solid phase dispersion for determination of fluoroquinolones, tetracyclines and sulfonamides in meat. Journal of Chromatography B, 1065 (2017) 104-111.

41. Wang, Y. Zhao, M.-N. Ou yang, H.-M. Guo, Z.-H. Yang, Magnetic polydopamine modified with deep eutectic solvent for the magnetic solid-phase extraction of sulfonylurea herbicides in water samples. Journal of Chromatography A, 1601 (2019) 53-59.

42. Wen, L., Liu, L., Wang, X., Wang, M. L., Lin, J. M., & Zhao, R. S. Spherical mesoporous covalent organic framework as a solid-phase extraction adsorbent for the ultrasensitive determination of sulfonamides in food and water samples by liquid chromatography-tandem mass spectrometry. Journal of Chromatography A, 1625 (2020).
43. Xia, Y. Dou, J. Gao, Y. Gao, W. Fan, G. Li, J. You, Adsorption behavior of a metal organic framework of University in Oslo 67 and its application to the extraction of sulfonamides in meat samples. Journal of Chromatography A, 1619 (2020) 460949.
44. Yang, H.J. Ni, C.L. Li, X.Y. Zhang, K. Wen, Y.B. Ke, H.J. Yang, W.M. Shi, S.X. Zhang, J.Z. Shen, Z.H. Wang, Development of a highly specific chemiluminescence aptasensor for sulfamethazine detection in milk based on in vitro selected aptamers. Sensors and Actuators B-Chemical, 281 (2019) 801-811.
45. Yao, K. Du, Simultaneous determination of sulfonamides in milk: In-situ magnetic ionic liquid dispersive liquid-liquid microextraction coupled with HPLC. Food Chemistry, 331 (2020) 127342.
46. Yazdanfar, N., Shamsipur, M., & Ghambarian, M. Determination of sulfonamide residues in animal foodstuffs by magnetic dispersive solid-phase extraction using magnetic carbon nanocomposites coupled with ion pair-dispersive liquid–liquid micro-extraction combined with HPLC-DAD. Journal of the Iranian Chemical Society, 18 (2021), 1433-1442.
47. Zhang, N., Gao, J., Huang, C., Liu, W., Tong, P., & Zhang, L. In situ hydrothermal growth of ZnO/g-C_3N_4 nanoflowers coated solid-phase microextraction fibers coupled with GC-MS for determination of pesticides residues. Analytica Chimica Acta, 934 (2016) 122-131.
48. Zhang, Y., Liao, W., Dai, Y., Wang, W., & Wang, A. Covalent organic framework Schiff base network-1-based pipette tip solid phase extraction of sulfonamides from milk and honey. Journal of Chromatography A, 1634 (2020) 461665.
49. Zhao, J.Y. Wang, J.P. Wang, S. Wang, Development of water-compatible molecularly imprinted solid-phase extraction coupled with high performance liquid chromatography-tandem mass spectrometry for the detection of six

sulfonamides in animal-derived foods. Journal of Chromatography A, 1574 (2018) 9-17.

50. Zheng, Y., Fan, L., Dong, Y., Li, D., Zhao, L., Yuan, X., et al. Determination of Sulfonamide Residues in Livestock and Poultry Manure Using Carbon Nanotube Extraction Combined with UPLC-MS/MS. Food Analytical Methods, 14 (2021) 641-652.
51. Zhong, Y.-H. Wang, L. Wang, R.-Q. Long, C.-L. Chen, Synthesis and characterization of magnetic molecularly imprinted polymers for enrichment of sanguinarine from the extraction wastewater of M. cordata. Journal of Industrial and Engineering Chemistry, 66 (2018) 107-115.

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A magnetic molecularly imprinted polymer hierarchical composite adsorbent embedded with a zinc oxide carbon foam nanocomposite for the extraction of sulfonamides

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ABSTRACT

A hierarchical composite adsorbent incorporated a nanocomposite of zinc oxide and carbon foam embedded in a magnetic molecularly imprinted polymer ($ZnO@CF@Fe_3O_4$-SiO_2-NH_2@MIP). The adsorbent was used to extract, preconcentrate and determine sulfonamides. The fabricated adsorbent was characterized, the fabrication and extraction conditions were investigated and the extracted sulfonamides were determined using high performance liquid chromatography. The zinc oxide carbon foam nanocomposite helped to improve the adsorption of sulfonamides. The MIP provided highly specific recognition cavities for three sulfonamides and the magnetic material enabled the simple and rapid separation of the adsorbent after adsorption and desorption. Under optimum conditions, the developed strategy provided a good linearity from 2.0 to 150.0 $\mu g\ L^{-1}$ with R^2 better than 0.995. The LOD and LOQ were 2.0 and 5.0 $\mu g\ L^{-1}$, respectively. The developed strategy determined sulfonamides in milk and water with extraction recoveries between 84.3 and 96.2% and RSDs lower than 7%. Concentrations of sulfadiazine were found in some milk and water samples at 2.50 and 2.05 $\mu g\ L^{-1}$, respectively. The advantages of the developed nanocomposite adsorbent are high specificity and extraction efficiency, simplicity and convenience, and good stability that enables reuse.

1. Introduction

Sulfonamides make up a group of medicines normally used as veterinary antibiotics to prevent infectious bacterial diseases and to support fish farming and animal husbandry [1]. An inevitable consequence of the wide use of these antibiotics is the presence of residual sulfonamides in animal products and the environment. The adverse effects of sulfonamides on humans can cause allergic reactions and damage to the urinary system. Owing to the excessive usage of sulfonamides, the residues in the food chain is becoming an increasingly serious problem [2]. The European Union has established the maximum residue limit (MRL) of 0.10 $mg\ kg^{-1}$ in animal-derived foods [3]. Water is also a very important constituent of ecosystem and its quality have to preserve and improve. Various organic and inorganic water pollutants have been reported such as pesticides [4,5], endocrine disruptor compounds [6], heavy metal and antibiotics [7]. Among the contaminant substances, sulfonamide antibiotics are also harmful effects on humans. Therefore, the determination of sulfonamides in foods and water is an important precaution.

Sulfonamides can be determined by chromatographic techniques [8,9,10], fluorescence spectroscopy [11], UV–Vis spectroscopy [12] and electrochemical [13,14]. Among these methods, high performance liquid chromatography (HPLC) is widely used. Since HPLC uses an analytical column which separates analytes before quantification, it is a highly selective method [15]. However, residual sulfonamides in food and environment are usually at trace levels which cannot be directly determined by instrumental analysis and must therefore be extracted and enriched beforehand. The extraction of sulfonamides can be achieved by solid phase extraction (SPE) [16,17], liquid–liquid microextraction (LLME) [12], deep eutectic solvents (DESs) [18] and magnetic solid-phase extraction (MSPE) [9]. MSPE is a simple procedure [19] which avoids the problems of conventional SPE, which is usually time-consuming and requires complicated manifold systems.

The extraction efficiency of target analytes are normally depends on the effectiveness of the adsorptive material [20]. Several adsorptive

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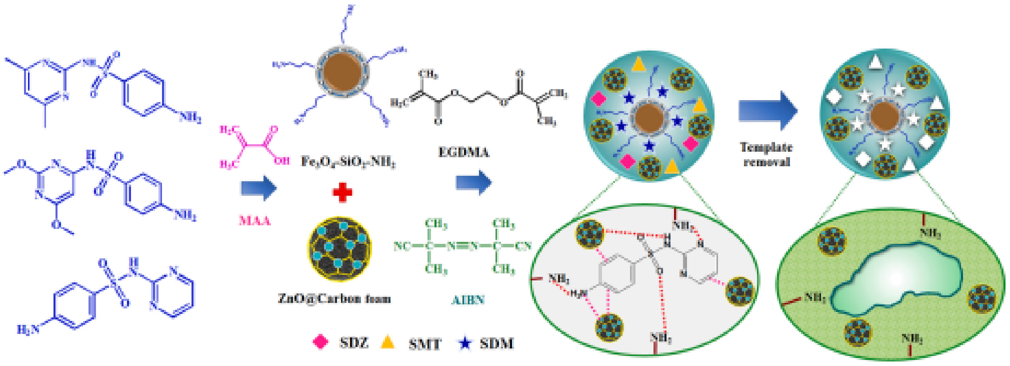

Fig. 1. The preparation procedure of the proposed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction of sulfonamides.

materials have been used for the adsorption of organic compounds especially nanomaterials [21,22,23] due to its large surface areas which can enhance the adsorption ability [24,25]. Various materials have been utilized to extract sulfonamides. These materials have included carbon nanotubes [26], polypyrrole [9], covalent organic frameworks [27,28], poly(ethylene glycol) diacrylate [16], molybdenum disulfide nanosheets [29] and graphitic carbon [30]. An interesting material for the extraction of sulfonamides in complex samples is molecularly imprinted polymer (MIP). MIPs are highly specific to target analytes and can reduce the co-adsorption of interferences in real samples. In addition, MIPs are easily synthesized and chemically stable. The selectivity of MIPs has been found useful in sensing probes [31], electrode modification for chemical sensors and adsorbents [32].

MIPs can be integrated with other materials to produce a composite adsorptive material with improved affinity for the target analytes. This is an attractive strategy for this work. Zinc oxide (ZnO) has been reported to effectively extract target compounds. However, it has poor dispersibility and readily aggregates [33]. ZnO incorporated with carbon foam (CF) is a more interesting material that has shown exciting potential for the extraction of target compounds due to it has a specific pore structure, a highly geometric surface area and good thermal stability. This composite material can adsorb sulfonamides via hydrophobic and π-π interactions and hydrogen bonding. The specificity of an MIP adsorbent can be improved by incorporating ZnO@CF.

In this work, a new magnetic molecularly imprinted polymer hierarchical nanocomposite embedded with a ZnO@CF was fabricated (ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP). It was developed for the first time for the extraction and enrichment of sulfonamides in milk and water samples. The developed hierarchical nanocomposite adsorbent was characterized and the fabrication strategy and extraction condition were optimized. The developed adsorbent was applied in the dispersive magnetic solid phase extraction (d-MSPE) of sulfonamides in milk and water to be determined by HPLC. The efficiency of the developed adsorbent was also compared with a commercial sorbent for the extraction of three sulfonamides, sulfamethazine (SMT), sulfadiazine (SDZ), and sulfadimethoxine (SDM).

2. Experimental

2.1. Chemical and reagents

Sucrose was obtained from Ajax Finechem (Australia). Zinc nitrate hexahydrate was from KEMAUS (Australia). Sulfamethazine (SMT), sulfadiazine (SDZ), sulfadimethoxine (SDM), ethylene glycol dimethacrylate (EGDMA), methacrylic acid (MAA), and 3-aminopropyltriethoxysilane (APTES) were from Tokyo Chemical Industry Co. Ltd (Tokyo, Japan). Iron (II) chloride and iron (III) chloride were from Sigma Aldrich (Steinheim, Germany). Alpha-azoisobutyronitrile (AIBN) was from BDH Chemicals (Lutterworth, UK). Acetone, acetonitrile, ethanol, acetic acid, and methanol were from RCI Labscan (Bangkok, Thailand).

2.2. Instrumentation

The HPLC analysis was performed in gradient mode on an 1100 series HPLC system (Agilent Technologies, Germany) equipped with a C18 (4.6 × 150 mm I.D., 5.0 μm) analytical column for the separation of target sulfonamides. The mobile phase was 0.02 % (v/v) acetic acid (A) and acetonitrile (B) at a flow rate of 1.0 mL min^{-1} with gradient elution as follows: 22–35% B; 0–5 min, 35–45% B; 5–8 min, 45–35% B; 8–10 min and 35–22% B; 10–12 min. The injection volume was 20 μL and the target sulfonamides were detected with a diode array detector (DAD) at 270 nm. The morphology was examined by scanning electron microscope (SEM), (Apreo FEI, Netherlands). The infrared spectra of the adsorbent and related materials were recorded by Fourier transform infrared spectrometer (Bruker, Germany). The crystalline phases of the adsorbent were determined by X-ray diffractometer (XRD) (Empreyan, PAN analytical, the Netherlands). Magnetic properties were determined with vibrating sample magnetometer (VSM) calibrated with a 3 mm diameter Ni sphere (Lakeshore 730908, USA). The surface areas were determined by a BET surface area analyzer (Model ASAP 2060 Micromeristic, USA).

2.3. Synthesis of Fe_3O_4-SiO_2-NH_2 nanoparticles

First, Fe_3O_4 was synthesized via a co-precipitation method in accordance with a previous report [34]. Briefly, 9.40 g $FeCl_3$·$6H_2O$ and 3.40 g $FeCl_2$·$4H_2O$ were dissolved in 150 mL of deionized (DI) water and transferred into a three-necked flask (250 mL). The solution was stirred under nitrogen at 80 °C for 10 min and 20 mL of ammonium hydroxide were added dropwise and stirring proceeded continuously for 1 h, at which point Fe_3O_4 nanoparticles were obtained. The nanoparticles were separated with a magnet, washed with DI water and dried at 70 °C for 5 h.

The Fe_3O_4-SiO_2-NH_2 nanoparticles were prepared by dispersing 0.50 g of the Fe_3O_4 nanoparticles in a 90 mL mixture solution of ethanol and DI water (1:1 v/v) under ultrasonication for 30 min. Then, 0.70 mL of APTES was added and adjusted to pH 4 with 1.0 M acetic acid. The reaction was performed for 3 h under stirring at 60 °C. The synthesized Fe_3O_4-SiO_2-NH_2 nanoparticles were washed with DI water and dried at 80 °C for 8 h.

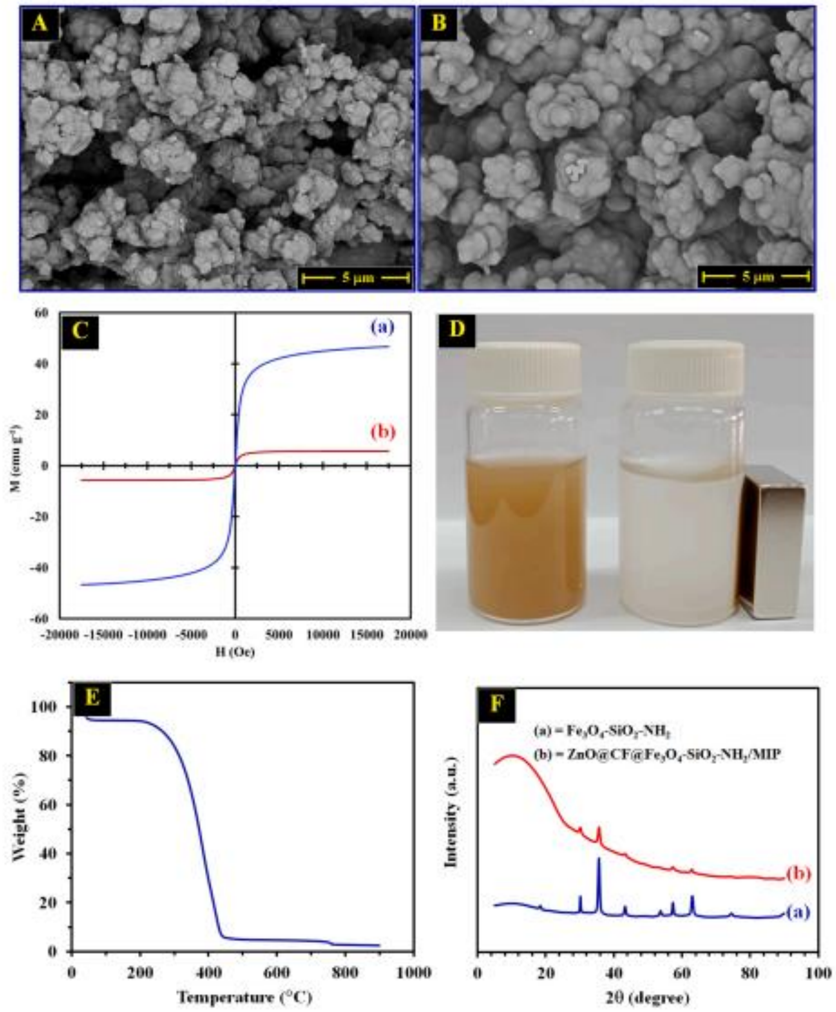

Fig. 2. SEM images of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP (A) and ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP (B): VSM curves (C) of (a) Fe_3O_4 and (b) ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP: Photograph of the dispersed composite adsorbent and the isolation of the adsorbent (D): TGA analysis curve (E) and XRD analysis (F).

2.4. Synthesis of zinc oxide incorporated carbon foam (ZnO@CF)

The ZnO@CF composite was prepared according to a previous report [35]. 3.0 g of sucrose and 1.50 g of $Zn(NO_3)_2{\cdot}6H_2O$ were combined in a beaker and heated to 110 °C. As the temperature increased, the mixture started to melt and was stirred with a glass rod and started to turn yellow, expand and foam. After further heating for 10 min, the foam turned black and the ZnO@CF composite was obtained. The synthesized ZnO@CF was stored in a desiccator until used.

2.5. Synthesis of hierarchical nanocomposite magnetic molecularly imprinted polymer

The hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was synthesized in the following procedure. First, 15.0 mg of SDZ, 17.0 mg of SMT and 19.0 mg of SDM were dissolved in 60 mL of acetonitrile. Then 90 µL of MAA were added to the sulfonamides solution and stirred for 12 h at 28 ± 1 °C. Subsequently, 100 mg of Fe_3O_4-SiO_2-NH_2 and 50 mg of ZnO@CF were added and stirred for 1 h. Then, 3.77 mL of EGDMA and 75.0 mg of AIBN were added into the solution. The polymerization was performed under N_2 at 60 °C for 24 h. The produced nanocomposite particle adsorbent was separated with a magnet and washed under stirring for 20 min with a mixture of acetic acid and methanol (2:8 v/v) to remove template. Finally, the fabricated ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was washed with 20 mL of DI water and dried at 80 °C for 8 h. A non-imprinted polymer (ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP) was also prepared under the same conditions but without the addition of the sulfonamide templates. Fig. 1 illustrated the fabrication procedure of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction of sulfonamides. Chemical structure of target sulfonamides are given in supporting information (**Fig. S1**).

2.6. *Dispersive magnetic solid phase extraction (d-MSPE)*

The d-MSPE extraction of sulfonamides using the fabricated adsorbent proceeded as follows: 50 mg of the adsorbent were dispersed in 15.0 mL of sample solution and stirred at 750 rpm for 30 min. After the adsorption of sulfonamides was completed, the adsorbent was separated using a magnet. The adsorbent particles were placed in 2.0 mL of a desorption solution of methanol and 1.0 M acetic acid (80:20 % v/v) and the adsorbed analytes were desorbed under sonication for 30 min. The adsorbent nanoparticles were separated with the magnet and the desorption solution was evaporated at 50 °C. Finally, the residue was dissolved in 1.0 mL of mobile phase, a mixture of 0.02% acetic acid and acetonitrile (78:22, v/v) and 20 μL was injected into the HPLC system.

3. Results and discussion

3.1. *Characterization of nanocomposite adsorbent and related materials*

The functional groups of ZnO@CF, Fe_3O_4-SiO_2-NH_2 and the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent were evaluated using FT-IR analysis. The FT-IR spectrum of ZnO@CF (**Fig. S2a**), shows a peak at 758 cm^{-1} from the Zn–O stretching vibration and a peak at 2952 cm^{-1} corresponding to the C–H bond vibration of carbon foam. These peaks confirm that ZnO@CF was successfully synthesized. The FT-IR spectrum of Fe_3O_4-SiO_2-NH_2 (**Fig. S2b**) presents an adsorption peak at 588 cm^{-1} due to the stretching of Fe-O, a peak at 1094 cm^{-1} from the stretching vibration of the Si—O—Si bond, and a peak at 3394 cm^{-1} corresponding to the stretching of the O—H bond. These characteristic peaks confirmed that the magnetic Fe_3O_4-SiO_2-NH_2 nanoparticles were successfully synthesized. In the FT-IR spectrum of the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (**Fig. S2c**), the absorption peaks at 3434 cm^{-1} and 1390 cm^{-1} are attributed to the C═N stretching vibration, indicating that the MIP was successfully formed. The characteristic peaks present in the spectra of ZnO@CF and Fe_3O_4-SiO_2-NH_2 are also present in the FT-IR spectrum of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent. The strong peak about 1600 cm^{-1} and broad peak between 3200 and 3600 cm^{-1} may be also due to the adsorption of water molecule during the measurement.

The SEM images of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP and ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP adsorbents in Fig. 2A and Fig. 2B show that the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent has a rougher surface than the NIP adsorbent. The difference in the surface morphologies is due to the formation of recognition sites on the MIP adsorbent.

The magnetic properties of Fe_3O_4 and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent were measured using the VSM technique. The saturation magnetizations of Fe_3O_4 nanoparticles and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP particles were 46.68 emu g^{-1} and 5.69 emu g^{-1}, respectively (Fig. 2C). Although the magnetic properties of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP particles was lower than the saturation magnetization of the Fe_3O_4 nanoparticles, the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent could nevertheless be easily isolated from the sample (Fig. 2D).

The thermal stability of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was determined by TGA analysis. The adsorbent exhibited good stability in the range of 25–200 °C (Fig. 2E). The thermal stability of the nanocomposite is therefore more than adequate for d-MSPE at room temperature.

The XRD patterns of Fe_3O_4-SiO_2-NH_2 and the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent both present diffraction peaks at 2θ angles of 30°, 36°, 54°, 63° and 74° corresponding to (220), (311), (422), (440), and (533) planes, respectively (Fig. 2F). These results are characteristic of crystalline cubic structures of Fe_3O_4 nanoparticles [36] and demonstrated Fe_3O_4-SiO_2-NH_2 with the MIP did not change their characteristics.

3.2. *Optimization of d-MSPE with the nanocomposite adsorbent*

To obtain a high extraction efficiency with low solvent consumption and rapid analysis time, the influences of parameters affecting d-MSPE with the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent were investigated. The parameters included the adsorbent dose, the extraction time, the desorption condition, the sample volume, the stirring rate during adsorption, the sample solution ionic strength and sample solution pH. The evaluation of extraction efficiency was based on extraction recovery, which was determined according to the equation, Extraction recovery (%) = $(C_S{}^*V_S/C_AV_A) \times 100$, where C_S is sulfonamides in the reconstituted solution, C_A is sulfonamides in a spiked water sample, and V_S and V_A are the volumes of the reconstituted solution and the spiked water sample, respectively.

3.2.1. *Adsorbent dose*

The amount, or dose, of an adsorbent is an important parameter that affects the adsorption of target analytes. The dose of the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was varied at 25, 50, 100, and 150 mg. The extraction recovery increased from 25 mg to 50 mg and remained constant at the higher doses (Fig. S3). Therefore, 50 mg of the proposed adsorbent was sufficient for effective recovery and was used for the extraction of sulfonamides.

3.2.2. *Extraction time*

Since the contact time between adsorbent and analytes is an important factor in the d-MSPE of analytes, the effect of contact time between the sulfonamides and the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was investigated. Contact time was varied from 10 to 60 min. The extraction recovery increased from 10 to 30 min and extraction recovery remained constant at longer extraction times (Fig. S4). Thus, the extraction of sulfonamides with the proposed adsorbent was performed for 30 min.

3.2.3. *Effect of type of desorption solvent*

Desorption of the three target sulfonamides from the nanocomposite adsorbent was performed with acetonitrile, ethyl acetate, acetone, methanol and a mixture of methanol and acetic acid. The mixture of methanol and 2.0 % acetic acid provided the best recovery (Fig. S5). The acidic condition can break hydrogen bonding and, therefore, may enable more complete desorption of sulfonamides from the nanocomposite adsorbent. At the same time, methanol can disrupt hydrophobic and π-π interactions. Therefore, methanol containing 2.0 % (v/v) acetic acid was the most effective desorption solvent investigated in this study.

3.2.4. *Effect of desorption solvent volume*

The effect of desorption solvent volume was also evaluated. The mixture of methanol and 2.0 % acetic acid was used at volumes of 1.0, 2.0, 4.0, and 6.0 mL. A volume of 2.0 mL was enough to desorb all three target sulfonamides from the nanocomposite adsorbent (Fig. S6). Therefore, 2.0 mL of desorption solvent was selected to desorb sulfonamides.

3.2.5. *Effect of desorption time*

The desorption of sulfonamides from the nanocomposite adsorbent was performed under ultrasonication. Therefore, sonication duration was optimized. Desorption was evaluated at ultrasonication times of 10,

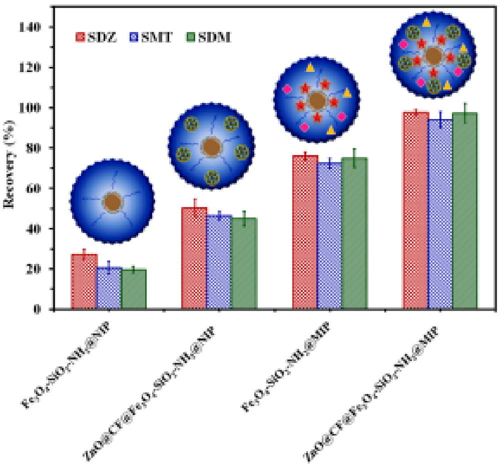

Fig. 3. Efficiency of different adsorbents for the extraction of sulfonamides.

20, 30, and 40 min using 2.0 mL of a mixture of methanol and 2% acetic acid. The recovery increased with time and reached a maximum at 30 min (Fig. S7), which implied that all adsorbed sulfonamides were completely desorbed from the hierarchical nanocomposite adsorbent. Thus, sonication was performed for 30 min to desorb the target sulfonamides from the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

3.2.6. Sample volume

The effect of the sample solution volume was investigated since it normally influences the extraction efficiency of analytes and the enrichment factor. Large sample volumes produce high enrichment factors, however, too large a sample volume can reduce the extraction efficiency of the adsorbent. In this work, the effects of sample volumes ranging from 5 to 20 mL were evaluated. The recovery of sulfonamides decreased when sample volume exceeded 15 mL (Fig. S8) since the ratio of adsorbent to sample volume was too low. Considering the enrichment factor and extraction recovery of sulfonamides, a sample volume of 15 mL was chosen.

3.2.7. Effect of stirring rate

The stirring rate of the sample solution typically affects the efficiency of d-MSPE. In this work, the stirring rate of the sample solution was varied from 500 to 1500 rpm. The extraction recovery was higher at 750 rpm than at 500 rpm and was lower at stirring rates above 750 rpm (Fig. S9). The reduced recovery at the higher stirring rates may be due to reduced contact between the adsorbent and target molecules. Moreover, higher stirring rates can damage adsorbents and affect reusability. Thus, the stirring rate of 750 rpm was selected for the adsorption of target sulfonamides with the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

3.2.8. Effect of ionic strength of sample solution

The ionic strength of the aqueous sample solution can affect the adsorption of sulfonamides by reducing solubility. In this work, the effect of ionic strength was investigated by adding different concentrations of NaCl to the sample solution. The NaCl concentrations were 0.0, 1.0, 2.0, 5.0 and 10.0 % w/v. Extraction recoveries increased with increments of NaCl up to 5.0 % w/v and decreased at 10.0 % w/v (Fig. S10) since sodium and chloride ions can disturb the binding between sulfonamides and recognition sites of the adsorbent. Thus, 5.0 % w/v NaCl was dissolved in the sample solution before sulfonamides were extracted with the proposed adsorbent.

3.2.9. Effect of sample pH

The effect of sample pH is an important consideration in the extraction process since the ionization and solubility of sulfonamides is affected by the pH of the sample solution. The sample pH was varied from 4 to 8 (Fig. S11). Recovery was lowest at pH 4 and was not significantly different from pH 5 to pH 8. The low recovery at pH 4 may be due to the disruption of analyte-adsorbent binding by hydrogen ions in the elevated acidic condition. However, in this work, the pH of milk and water samples was between 5 and 8, and therefore sample pH adjustment was not required.

3.3. Type of adsorbent

We compared the extraction efficiency of different types of molecularly non-imprinted and molecularly imprinted polymer magnetic nanocomposite adsorbent. The studied types included Fe_3O_4-SiO_2-NH_2@NIP, ZnO@CF@Fe_3O_4-SiO_2-NH_2@NIP, Fe_3O_4-SiO_2-NH_2@MIP, and ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbents (Fig. 3). The NIP adsorbents achieved lower extraction recoveries than the MIP adsorbents since, unlike the MIP adsorbents, they did not have specific recognition sites for sulfonamides. The Fe_3O_4-SiO_2-NH_2@NIP adsorbent can adsorb target sulfonamides only via hydrogen bonding between functionalized NH_2 group on the surface of adsorbent and target sulfonamides. The ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP achieved higher recoveries than the Fe_3O_4-SiO_2-NH_2@MIP. The incorporated ZnO@CF nanocomposite improved the extraction efficiency of the adsorbent toward the target sulfonamides, and therefore the nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was the most suitable of the present materials for the extraction of sulfonamides.

3.4. Comparison with C18 sorbent

The extraction efficiency of the ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent toward the target sulfonamides was compared with the efficiency of a commercial C18 sorbent. The proposed adsorbent achieved recoveries from 91.6 to 96.0 % and the C18 adsorbent achieved recoveries from 85.7 to 88.0% (Fig. S12). However, the developed adsorbent (50 mg) requires less amount of adsorbent than commercial C18 sorbent (500 mg). In addition, the extraction procedure of the developed magnetic adsorbent is easier, faster and can be reused which reduces analysis cost. The developed adsorbent performs well and has excellent selectivity. The developed adsorbent can be applied to determine sulfonamides in complex samples.

3.5. Adsorption kinetics

Pseudo-first-order (PFO) and pseudo-second-order (PSO) models were applied to evaluate the adsorption kinetics between the developed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent and the target sulfonamides. The PFO model describes the adsorption of sulfonamides onto the nanocomposite adsorbent according to the following equation:

$$log(q_e - q_t) = log\, q_e - -\frac{k_1}{2.303}t$$

By plotting log ($q_e - q_t$) versus t, k_1 and q_e can be estimated from the slope and intercept, respectively.

The PSO model is based on the amount of sulfonamides on the nanocomposite adsorbent according to following equation:

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

Table 1
The analytical performances for the extraction and determination of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent and high performance liquid chromatography.

Analytes	Linear range	Calibration curve	R^2	LOD (μg L^{-1})	LOQ (μg L^{-1})	Enrichment factor	Repeatability	
							Intra-day (n = 6) (RSD %)	Inter-day (n = 6) (RSD %)
SDZ	2.0–150	y = 0.0440x-0.0006	0.9975	2.0	5.0	12.6	4.0	5.4
SMT	2.0–150	y = 0.0646x-0.0440	0.9996	2.0	5.0	12.8	3.4	5.0
SDM	2.0–150	y = 0.0867x-0.0721	0.9987	2.0	5.0	13.9	4.4	5.4

Table 2
Three sulfonamides in milk and water samples were extracted using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent and determined with high performance liquid chromatography.

Sample	Added μg L^{-1}	SDZ			SMT			SDM		
		F (μg L^{-1})	RR (%)	RSD (%)	F (μg L^{-1})	RR (%)	RSD (%)	F (μg L^{-1})	RR (%)	RSD (%)
Milk 1	0.00	–	–	–	–	–	–	–	–	–
	10.0	8.43	84.3	5.9	8.55	85.5	5.1	9.26	92.6	5.3
	20.0	18.12	91.0	4.8	17.21	86.0	4.8	18.90	94.5	5.1
	50.0	46.90	93.8	2.9	42.89	85.8	3.9	48.10	96.2	2.9
Milk 2	0.00	–	–	–	–	–	–	–	–	–
	10.0	8.44	84.4	4.8	9.30	93.0	5.9	9.01	90.1	4.0
	20.0	18.39	91.9	3.9	17.42	87.1	4.6	18.45	92.3	3.8
	50.0	45.20	90.4	2.4	43.98	88.0	3.0	46.10	92.2	1.8
Milk 3	0.00	2.50	–	5.0	–	–	–	–	–	–
	10.0	11.89	93.9	4.8	9.03	90.3	5.6	8.67	86.7	5.0
	20.0	21.09	93.0	4.5	18.90	94.5	4.8	17.90	89.5	4.3
	50.0	49.80	94.6	4.0	46.09	92.2	4.6	45.98	92.0	2.6
Water 1	0.00	2.05	–	4.0	–	–	–	–	–	–
	10.0	11.05	90.0	3.8	8.67	86.7	4.0	8.90	89.0	4.2
	20.0	20.10	90.2	3.5	17.87	89.4	3.7	18.08	90.4	2.6
	50.0	50.05	96.0	3.5	46.80	93.6	3.8	47.0	94.0	3.0
Water 2	0.00	–	–	–	–	–	–	–	–	–
	10.0	8.69	86.9	6.0	8.65	86.5	5.9	8.90	89.0	6.2
	20.0	18.21	91.1	4.8	19.03	95.1	4.5	17.43	87.1	3.9
	50.0	45.90	91.8	3.0	45.89	91.8	4.0	45.00	90.0	4.0
Water 3	0.00	–	–	–	–	–	–	–	–	–
	10.0	8.78	87.8	5.8	8.56	85.6	4.6	8.68	86.8	5.6
	20.0	17.89	89.4	4.8	17.08	85.4	4.2	18.08	90.4	3.8
	50.0	45.60	91.2	4.5	45.89	91.8	4.3	47.05	94.1	3.6

where q_t (mg g^{-1}) is the amount of adsorbed analyte at a given time and q_e (mg g^{-1}) is the equilibrium adsorption capacity. By plotting t/qt versus t, k_2 and q_e are acheived from the intercept and slope, respectively.

It can be seen that the coefficient of determination ($R^2 > 0.999$) of fitting with the PSO model are better than the R^2 values of fitting with the PFO model **(Table S1)**. These results confirmed that the adsorption kinetics are governed by chemisorption.

3.6. *Analytical performances*

The analytical performances of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent coupled with HPLC-DAD were evaluated including linearity, LOD, LOQ, enrichment factor (EF) and repeatability. The results are presented in Table 1. The LOD and LOQ of the developed method were estimated to be 2.0 and 5.0 μg L^{-1}, based on signal-to-noise ratios of 3 and 10, respectively. Enrichment factors were determined from the ratio of the concentration of each sulfonamide after extraction to the initial concentration of each sulfonamide in the sample solution ($EF = C_{MSPE}/C_0$). The evaluation of the repeatability was based on intra-day and inter-day precision and the RSD were investigated within one day and six different days, respectively. These results indicated the high sensitivity and outstanding repeatability of the developed approach.

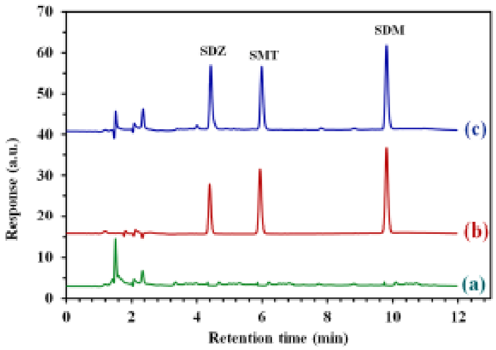

Fig. 4. Chromatograms show sulfonamides extracted from a real milk sample (a), standard sulfonamides solution (b), and a spiked milk sample (c), using the proposed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

3.7. *Analysis of sulfonamides in milk and water*

The developed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was applied to extract and determine sulfonamides in milk and aquaculture water samples. Concentrations of sulfadiazine

Table 3
The analytical method for the determination of sulfonamides in various samples.

Extraction method	Method	Extractant	Sample	Sample amount	Elution volume (mL)	LOD ($\mu g\ L^{-1}$)	Recovery (%)	References
MSPE	HPLC-DAD	Fe_3O_4–GOx	Water	1 mL	1	0.05–0.10	67.4–119.9	[37]
MSPE	HPLC-UV	$CoFe_2O_4$-graphene	Milk	1.5 mL	0.5	1.16–1.59	62.0–104.3	[38]
MSPE	HPLC-UV	MIP-pGMA@A-MNPs	Feed	7 g	2	16	89.3–107.0	[39]
SLE	HPLC-DAD	MeOH and ACN	Shrimp	1 g	0.5	8.4–10.9	81.6–116.8	[8]
SPE	HPLC-DAD	Sol-gel/MIP	Milk	1 g	2	1.9–13.3	85.8–109.2	[40]
SPE	HPLC-UV	MIP	Soil	10 mL	1	1.0	95.0–105.0	[41]
SPE	HPLC-DAD	VTTS-MGO@mSiO_2/MIP	Water	50 mL	2	0.010–0.014	87.4–102.3	[42]
d-MSPE	HPLC-UV	YS-Fe_3O_4@GC	Milk	25 mL	1.8	0.11–0.25	77.2–118.0	[30]
MSPE-i- DLLME	HPLC-DAD	MCNs	Food stuffs	100 mL	1	0.01–5.00	70.0–90.0	[10]
MSPE	HPLC-DAD	ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP	Milk and water	15 mL	2	2.0	84.3–96.2	This work

MSPE = magnetic solid-phase extraction, SLE = solid–liquid extraction, SPE = solid-phase extraction, d-MSPE = dispersive magnetic solid-phase extraction, DLLME = liquid–liquid micro-extraction: DAD = diode array detection, UV = ultra-violet detection, Fe_3O_4–GOx = Fe_3O_4–graphene oxide, $CoFe_2O_4$-graphene = graphene-based magnetic nanocomposite, MIP = molecularly imprinted polymer, pGMA = poly(glycidyl methacrylate), A-MNPs = amino-functionalized magnetic nanoparticles, MGO@mSiO_2 = magnetic graphene oxide, VTTS-MGO@mSiO_2 = magnetic graphene oxide modified with vinyl groups, LPME = liquid-phase microextraction, YS-Fe_3O_4@GC = yolk-shell Fe_3O_4@graphitic carbon, MCNs = magnetic carbon nanocomposite.

lower than the maximum residue limits were found in some samples (Table 2). The accuracy was also evaluated by spiking sulfonamides in real samples at 10, 20 and 50 $\mu g\ L^{-1}$. Accuracy was evaluated in terms of relative recovery, which was determined according to the following equation:

Relative recovery (%) = $(C_T\text{-}C_S)/C_{Spike}$ *100, where C_T is the total sulfonamides in the sample after spiking with the standard, C_S is the residual sulfonamides in the sample, and C_{Spike} is the sulfonamides spiked in the sample. The obtained relative recoveries from the milk ranged from 84.3 to 96.2 % and the water samples ranged from 85.4 to 96.0 %. The RSDs ranged from 2.4 to 6.2%. The HPLC chromatograms for a milk sample, standard sulfonamides, and a spiked milk sample (Fig. 4) were produced after extraction using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent.

3.8. Reusability of hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

The reusability of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent was investigated by the repeated extraction of sulfonamides in milk. To eliminate any carry-over effect, the used adsorbent was cleaned before the next extraction by washing with 2.0 mL methanol and DI water. The developed adsorbent can be reused 5 times before the recovery of sulfonamides falls below 80 % (Fig. S13). The decreasing extraction recovery after 5 extraction cycles due to the loss of adsorption material during the washing step and the possible adsorption through non-specific interaction of some interferences. The developed composite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction of sulfonamides in real samples can be effectively used for 5 adsorption–desorption cycles.

3.9. Comparison with other works

The analytical performances of the developed approach were compared with those of other methods previously reported for the extraction and determination of sulfonamides. The comparison is summarized in Table 3. The developed method provided comparable or better extraction recoveries than other methods. The LOD is also comparable with other methods. In addition, the developed nanocomposite adsorbent is highly specific for sulfonamides which enables its application in a variety of matrix samples. Thus, the developed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent presents a highly effective and selective alternative method of extracting sulfonamides, which is also simple, rapid and convenient to perform.

4. Conclusion

A novel hierarchical nanocomposite adsorbent was successfully designed and fabricated using zinc oxide, carbon foam, silica-coated magnetite nanoparticles, and molecularly-imprinted polymer. The fabricated adsorbent was utilized to extract and determine sulfonamides in milk and aquaculture water samples. The nanocomposite of zinc oxide and carbon foam exhibited a high adsorption ability, the molecularly-imprinted polymer was highly specific toward the target sulfonamides. The developed method achieved good recoveries (84.3–96.2 %) of sulfonamides and exhibited good selectivity, reproducibility and repeatability. The nanocomposite adsorbent is simple to fabricate, convenient to use, rapid, and its stability allows reuse. The developed approach can be modified and utilized to extract and determine other compounds in various sample matrices.

CRediT authorship contribution statement

Ananya Kliangsuwan: Methodology, Software, Validation, Writing – original draft, Conceptualization. **Apichai Phonchai:** Conceptualization, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing. **Opas Bunkoed:** Methodology, Conceptualization, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

[1] X.Z. Shi, Y. Meng, J.H. Liu, A.L. Sun, D.X. Li, C.X. Yao, Y. Lu, J. Chen, Group-selective molecularly imprinted polymer solid-phase extraction for the simultaneous determination of six sulfonamides in aquaculture products, J. Chromatogr. B 879 (2011) 1071–1076, https://doi.org/10.1016/j.jchromb.2011.03.019.

[2] A.G. Ayankojo, J. Reut, A. Opik, V. Syritski, Sulfamethizole-imprinted polymer on screen-printed electrodes: towards the design of a portable environmental sensor, Sens. Actuators B Chem. 320 (2020) 9, https://doi.org/10.1016/j.snb.2020.128600.

[3] M. Conde-Cid, G. Ferreira-Coelho, D. Fernandez-Calvino, A. Nunez-Delgado, M. J. Fernandez-Sanjurjo, M. Arias-Estevez, E. Alvarez-Rodriguez, Single and simultaneous adsorption of three sulfonamides in agricultural soils: Effects of pH and organic matter content, Sci. Total Environ. 744 (2020) 14, https://doi.org/10.1016/j.scitotenv.2020.140872.

[4] A.A. Basheer, Chemical chiral pollution: impact on the society and science and need of the regulations in the 21st century, Chiral J. 30 (2018) 402–406, https://doi.org/10.1002/chir.22808.

[5] I. Ali, C.K. Jain, Groundwater contamination and health hazards by some of the most commonly used pesticides, Curr. Sci. 75 (1998) 1011–1014. http://www.jstor.org/stable/24101777.

[6] A.A. Basheer, New generation nano-adsorbents for the removal of emerging contaminants in water, J. Mol. Liq. 261 (2018) 583–593.

[7] A.A. Basheer, I. Ali, Stereoselective uptake and degradation of (±)-o, p-DDD pesticide stereomers in water-sediment system, Chiral J. 30 (2018) 1088–1095, https://doi.org/10.1002/chir.22989.

[8] S. Charitonos, V.F. Samanidou, I. Papadoyannis, Development of an HPLC-DAD method for the determination of five sulfonamides in shrimps and validation according to the European Decision 657/2002/EC, Food Anal. Methods 10 (2017) 2011–2017, https://doi.org/10.1007/s12161-016-0766-1.

[9] T. Sukchuay, P. Kanatharana, R. Wannapob, P. Thavarungkul, O. Bunkoed, Polypyrrole/silica/magnetite nanoparticles as a sorbent for the extraction of sulfonamides from water samples, J. Sep. Sci. 38 (2015) 3921–3927, https://doi.org/10.1002/jssc.201500766.

[10] N. Yazdanfar, M. Shamsipur, M. Ghambarian, Determination of sulfonamide residues in animal foodstuffs by magnetic dispersive solid-phase extraction using magnetic carbon nanocomposites coupled with ion pair-dispersive liquid–liquid micro-extraction combined with HPLC-DAD, J. Iran. Chem. Soc. 18 (2021) 1433–1442, https://doi.org/10.1007/s13738-020-02127-2.

[11] N. Orachorn, O. Bunkoed, Nanohybrid magnetic composite optosensing probes for the enrichment and ultra-trace detection of mafenide and sulfisoxazole, Talanta 228 (2021) 122237, https://doi.org/10.1016/j.talanta.2021.122237.

[12] F. Shakirova, A. Shishov, 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 234 (2021) 122660, https://doi.org/10.1016/j.talanta.2021.122660.

[13] M. Li, B. He, Ultrasensitive sandwich-type electrochemical biosensor based on octahedral gold nanoparticles modified poly (ethylenimine) functionalized graphitic carbon nitride nanosheets for the determination of sulfamethazine, Sens. Actuators B Chem. 329 (2021), 129158, https://doi.org/10.1016/j.snb.2020.129158.

[14] J. Melo Henrique, J. Rocha Camargo, G. Gabriel de Oliveira, J. Santos Stefano, B. Campos Janegitz, Disposable electrochemical sensor based on shellac and graphite for sulfamethoxazole detection, Microchem. J. 170 (2021) 106701, https://doi.org/10.1016/j.microc.2021.106701.

[15] X. Geng, S. Lv, J. Yang, S. Cui, Z. Zhao, Carboxyl-functionalized biochar derived from walnut shells with enhanced aqueous adsorption of sulfonamide antibiotics, J. Environ. Manage. 280 (2021) 111749, https://doi.org/10.1016/j.jenvman.2020.111749.

[16] A. Moga, M. Vergara-Barberán, M.J. Lerma-García, J.M. Herrero-Martínez, E. F. Simó-Alfonso, Poly(ethylene glycol) diacrylate-based solid-phase extraction for determination of sulfonamides in meat samples, Microchem. J. 157 (2020) 104931, https://doi.org/10.1016/j.microc.2020.104931.

[17] L. Wen, L. Liu, X. Wang, M.L. Wang, J.M. Lin, R.S. Zhao, Spherical mesoporous covalent organic framework as a solid-phase extraction adsorbent for the ultrasensitive determination of sulfonamides in food and water samples by liquid chromatography-tandem mass spectrometry. J. Chromatogr. A 1625 (2020) 461275, https://doi.org/10.1016/j.chroma.2020.461275.

[18] A. Shishov, A. Gorbunov, E. Baranovskii, A. Bulatov, Microextraction of sulfonamides from chicken meat samples in three-component deep eutectic solvent, Microchem. J. 158 (2020) 105274, https://doi.org/10.1016/j.microc.2020.105274.

[19] S. Jullakan, O. Bunkoed, A nanocomposite adsorbent of metallic copper, polypyrrole, halloysite nanotubes and magnetite nanoparticles for the extraction and enrichment of sulfonamides in milk, J. Chromatogr.B. 1180 (2021) 122900, https://doi.org/10.1016/j.jchromb.2021.122900.

[20] P.I. Ali, T.A. Khan, I. Ahmad, Treatment and remediation methods for arsenic removal from the ground water, Int. J. Environ. Eng. 3 (2011) 48–71, https://doi.org/10.1504/IJEE.2011.037873.

[21] A.A. Basheer, Advances in the smart materials applications in the aerospace industries, Aircr Eng Aerosp Technol. 92 (2020) 1027–1035, https://doi.org/10.1108/AEAT-02-2020-0040.

[22] I. Ali, O.M.L. Alharbi, Z.A. Alothman, A. Alwarthan, A.M. Al-Mohaimeed, Preparation of a carboxymethylcellulose-iron composite for uptake of atorvastatin in water, Int. J. Biol. Macromol. 132 (2019) 244–253, https://doi.org/10.1016/j.ijbiomac.2019.03.211.

[23] P.I. Ali, O. Alharbi, Z. Alothman, A. Badjah-Hadj-Ahmed, Kinetics, thermodynamics, and modeling of amido black dye photodegradation in water using Co/TiO_2 nanoparticles, J Photochem Photobiol. 94 (2018) 935-941. https://doi.org/10.1111/php.12937.

[24] P.I. Ali, A. Burakov, A. Melezhik, A. Babkin, I. Burakova, E. Neskoromnaya, E. Galunin, A. Tkachev, D. Kuznetsov, Removal of copper(II) and zinc(II) ions in water on a newly synthesized polyhydroquinone/graphene nanocomposite material: kinetics, thermodynamics and mechanism, Chem. Select. 4 (2019) 12708–12718, https://doi.org/10.1002/slct.201902657.

[25] N. Al-Shaalan, P.I. Ali, Z. Alothman, L. Al-Wahaibi, H. Alabdulmonem, High performance removal and simulation studies of diuron pesticide in water on MWCNTs, J. Mol. Liq. 289 (2019), 111039, https://doi.org/10.1016/j.molliq.2019.111039.

[26] Y. Zheng, L. Fan, Y. Dong, D. Li, L. Zhao, X. Yuan, L. Wang, S. Zhao, Determination of sulfonamide residues in livestock and poultry manure using carbon nanotube extraction combined with UPLC-MS/MS, Food Anal. Methods 14 (2021) 641–652, https://doi.org/10.1007/s12161-020-01910-4.

[27] Y. Zhang, W. Liao, Y. Dai, W. Wang, A. Wang, Covalent organic framework Schiff base network-1-based pipette tip solid phase extraction of sulfonamides from milk and honey, J. Chromatogr. A 1634 (2020) 461665, https://doi.org/10.1016/j.chroma.2020.461665.

[28] D. Lu, C. Liu, M. Qin, J. Deng, G. Shi, T. Zhou, Functionalized ionic liquids-supported metal organic frameworks for dispersive solid phase extraction of sulfonamide antibiotics in water samples, Anal. Chim. Acta 1133 (2020) 88–98, https://doi.org/10.1016/j.aca.2020.07.074.

[29] Y. Li Juan, Z.X. Ci Dan, Q.G. Liao, Z. Da Wen, L. Lin Guang, Pipette-tip solid-phase extraction using cetyltrimethylammonium bromide enhanced molybdenum disulfide nanosheets as an efficient adsorbent for the extraction of sulfonamides in environmental water samples, J. Sep. Sci. 43 (2020) 905–911, https://doi.org/10.1002/jssc.201900871.

[30] X. Liu, Y. Tong, L. Zhang, Tailorable yolk-shell Fe_3O_4@graphitic carbon submicroboxes as efficient extraction materials for highly sensitive determination of trace sulfonamides in food samples, Food Chem. 303 (2020) 125369, https://doi.org/10.1016/j.foodchem.2019.125369.

[31] N. Chansud, N. Longnapa, O. Bunkoed, A nanohybrid magnetic sensing probe for levofloxacin determination integrates porous graphene, selective polymer and graphene quantum dots, J. Pharm. Biomed. Anal. 205 (2021) 114316, https://doi.org/10.1016/j.jpba.2021.114316.

[32] M. Nurrokhimah, P. Nurerk, P. Kanatharana, O. Bunkoed, A nanosorbent consisting of a magnetic molecularly imprinted polymer and graphene oxide for multi-residue analysis of cephalosporins, Microchim. Acta 186 (2019) 9, https://doi.org/10.1007/s00604-019-3985-5.

[33] N. Zhang, J. Gao, C. Huang, W. Liu, P. Tong, L. Zhang, In situ hydrothermal growth of ZnO/g-C_3N_4 nanoflowers coated solid-phase microextraction fibers coupled with GC-MS for determination of pesticides residues, Anal. Chim. Acta 934 (2016) 122–131, https://doi.org/10.1016/j.aca.2016.06.029.

[34] W. Kaewsuwan, P. Kanatharana, O. Bunkoed, Dispersive magnetic solid phase extraction using octadecyl coated silica magnetite nanoparticles for the extraction of tetracyclines in water samples, J. Anal. Chem. 72 (2017) 957–965, https://doi.org/10.1134/S1061934817090143.

[35] M. Sajid, C. Basheer, M. Mansha, Membrane protected micro-solid-phase extraction of organochlorine pesticides in milk samples using zinc oxide incorporated carbon foam as sorbent, J. Chromatogr. A 1475 (2016) 110–115, https://doi.org/10.1016/j.chroma.2016.11.008.

[36] N.K. Yetim, F.K. Baysak, M.M. Koç, D. Nartop, Characterization of magnetic Fe_3O_4@SiO_2 nanoparticles with fluorescent properties for potential multipurpose imaging and theranostic applications, J. Mater. Sci.: Mater. Electron. 31 (2020) 18278–18288, https://doi.org/10.1007/s10854-020-04375-7.

[37] P. Shi, N. Ye, Magnetite–graphene oxide composites as a magnetic solid-phase extraction adsorbent for the determination of trace sulfonamides in water samples, Anal. Methods 6 (2014) 9725–9730, https://doi.org/10.1039/C4AY02027H.

[38] Y. Li, X. Wu, Z. Li, S. Zhong, W. Wang, A. Wang, J. Chen, Fabrication of $CoFe_2O_4$–graphene nanocomposite and its application in the magnetic solid phase extraction of sulfonamides from milk samples, Talanta 144 (2015) 1279–1286, https://doi.org/10.1016/j.talanta.2015.08.006.

[39] M. Feng, H.Y. Li, L. Zhang, J.Y. Zhang, J.P. Dai, X.J. Wang, L.L. Zhang, Y.J. Wei, Preparation and application of novel magnetic molecularly imprinted composites for recognition of sulfadimethoxine in feed samples, Anal. Sci. 32 (2016) 517–521, https://doi.org/10.2116/analsci.32.517.

[40] M. Kechagia, V. Samanidou, A. Kabir, K.G. Furton, One-pot synthesis of a multi-template molecularly imprinted polymer for the extraction of six sulfonamide residues from milk before high-performance liquid chromatography with diode

array detection, J. Sep. Sci. 41 (2018) 723–731, https://doi.org/10.1002/jssc.201701205.

[41] G.F. Zhu, W.W. Li, L. Wang, P.Y. Wang, D.Y. Shi, J.J. Wang, J. Fan, Using ionic liquid monomer to improve the selective recognition performance of surface imprinted polymer for sulfamonomethoxine in strong polar medium, J. Chromatogr. A 1592 (2019) 38–46, https://doi.org/10.1016/j.chroma.2019.01.053.

[42] Y.M. Fan, G.L. Zeng, X.G. Ma, Effects of prepolymerization on surface molecularly imprinted polymer for rapid separation and analysis of sulfonamides in water, J. Colloid Interface Sci. 571 (2020) 21–29, https://doi.org/10.1016/j.jcis.2020.03.027.

Supplementary material

A magnetic molecularly imprinted polymer hierarchical composite adsorbent embedded with a zinc oxide carbon foam nanocomposite for the extraction of sulfonamides

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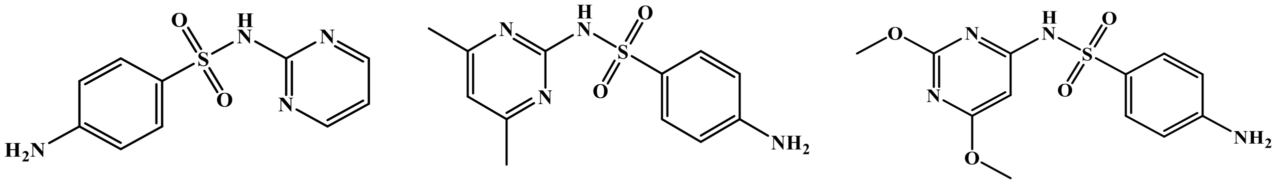

Sulfadiazine, SDZ

Sulfamethazine, SMT

Sulfadimethoxine, SDM

Fig. S1 Chemical structure of three target sulfonamides (sulfadiazine, sulfamethazine, sulfadimethoxine)

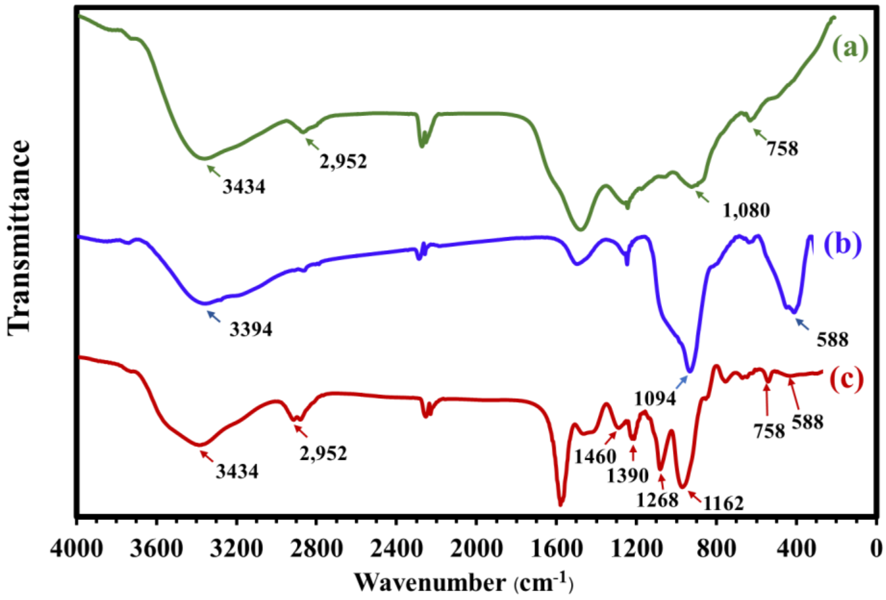

Fig. S2 FT-IR spectra of ZnO@CF (a), Fe_3O_4-SiO_2-NH_2 (b) and the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (c)

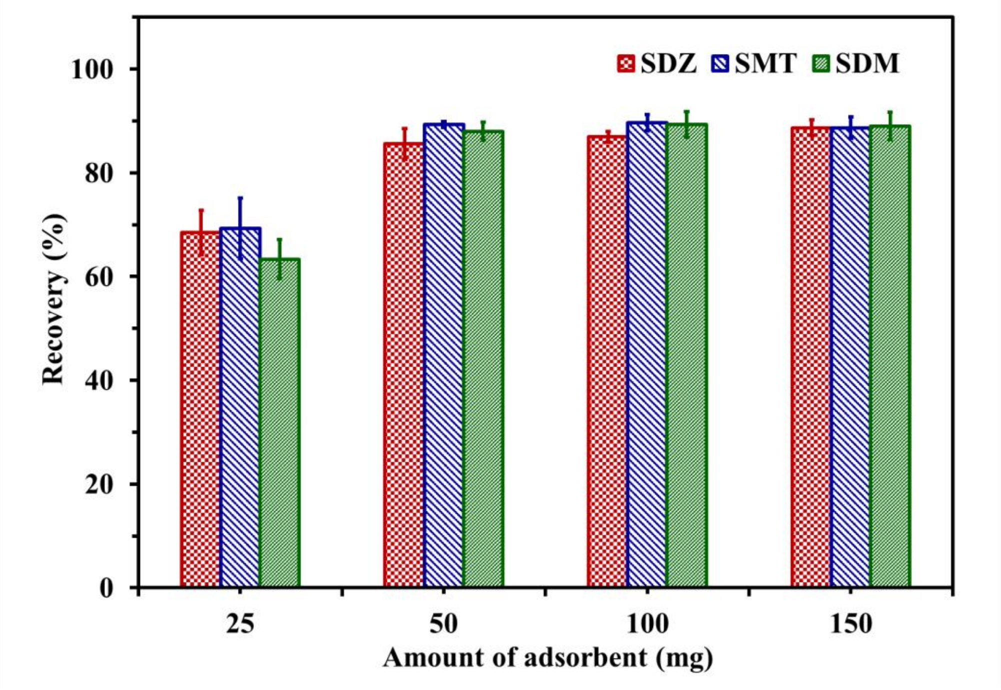

Fig. S3 Effect of the hierarchical nanocomposite ZnO@CF@Fe_3O_4@SiO_2-NH_2@MIP adsorbent dosage on the extraction of sulfonamides (n=3).

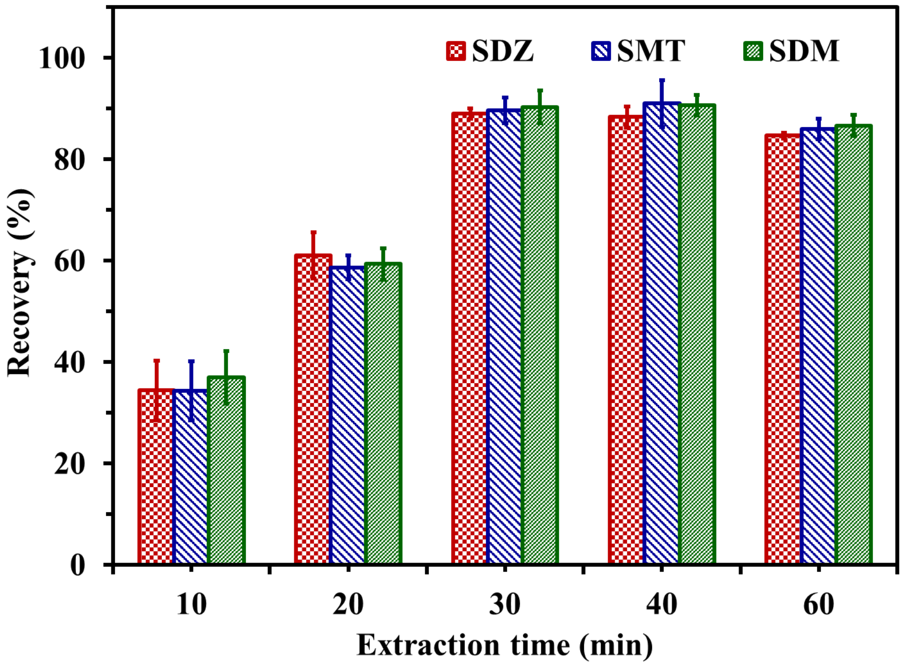

Fig. S4 Effect of extraction time on the recovery of target sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

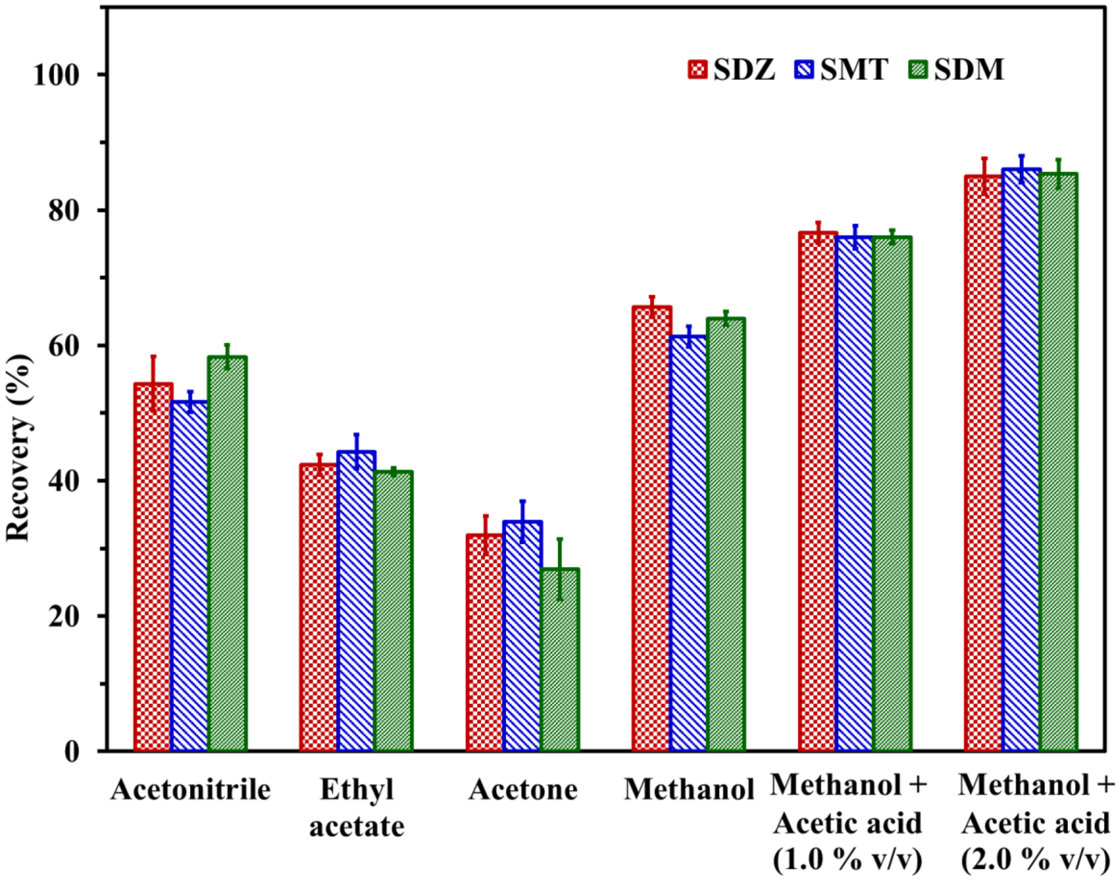

Fig. S5 Effect of the type of desorption solvent on the recovery of sulfonamides with the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

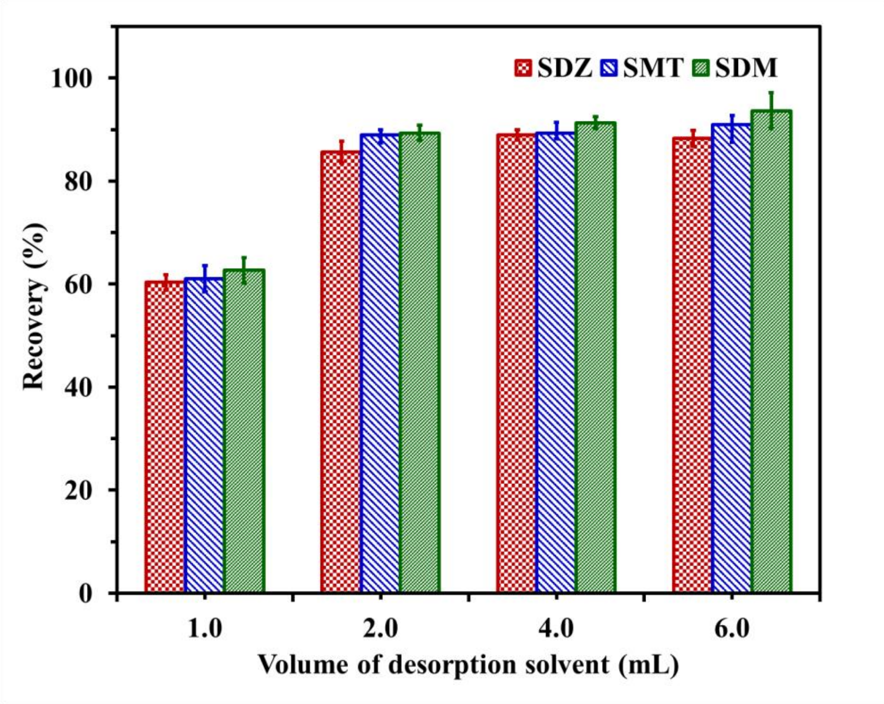

Fig. S6 Effect of desorption solvent volume on the desorption of sulfonamides from the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

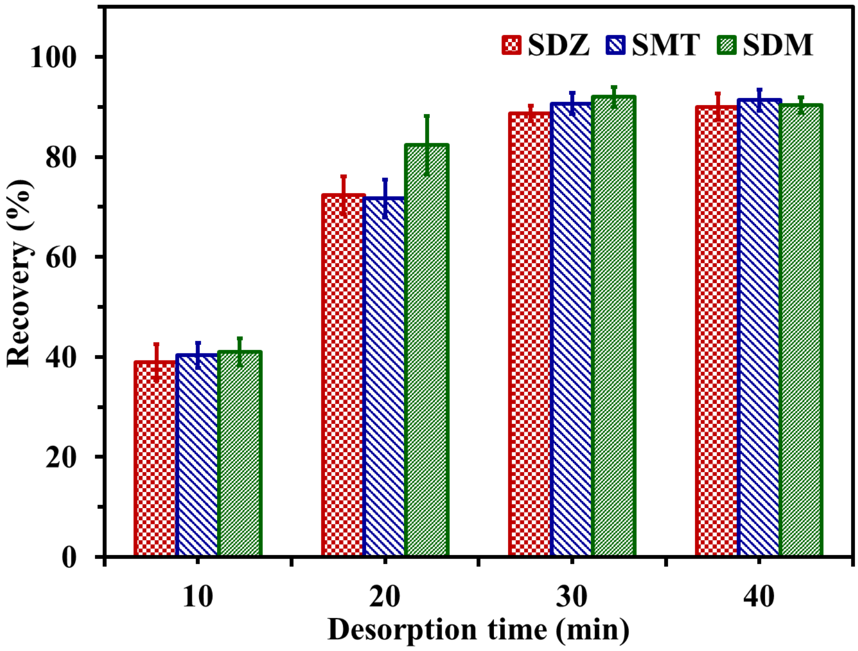

Fig. S7 Effect of sonication time on the desorption of adsorbed sulfonamides from the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

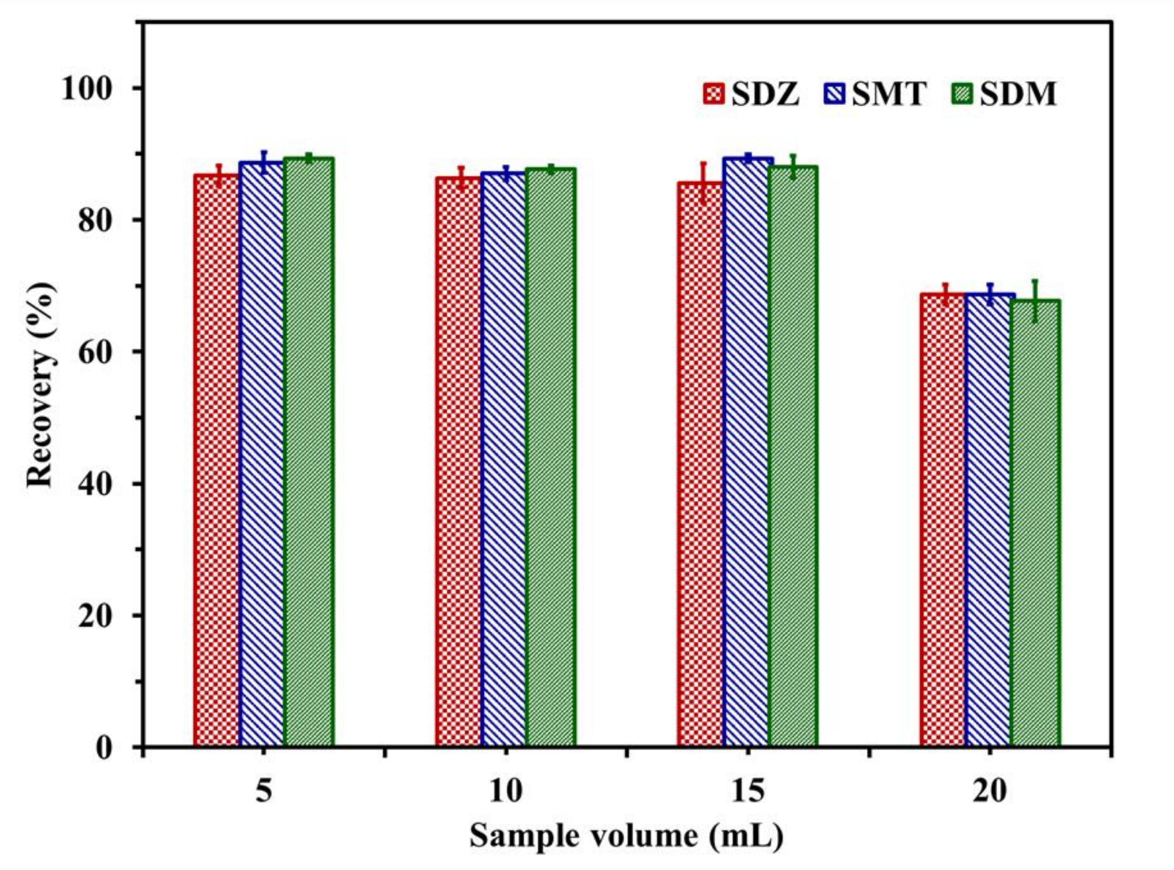

Fig. S8 Effect of sample solution volume on the extraction of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

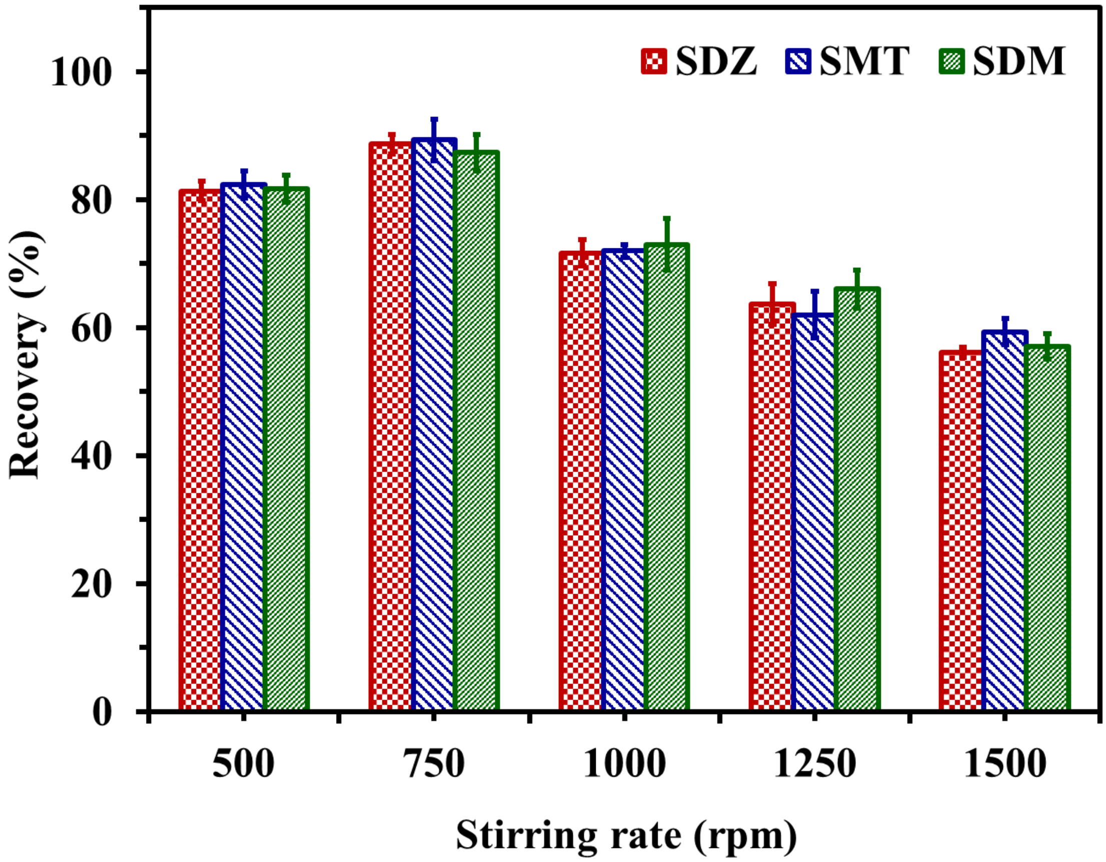

Fig. S9 Effect of solution stirring rate on the adsorption of sulfonamides on the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

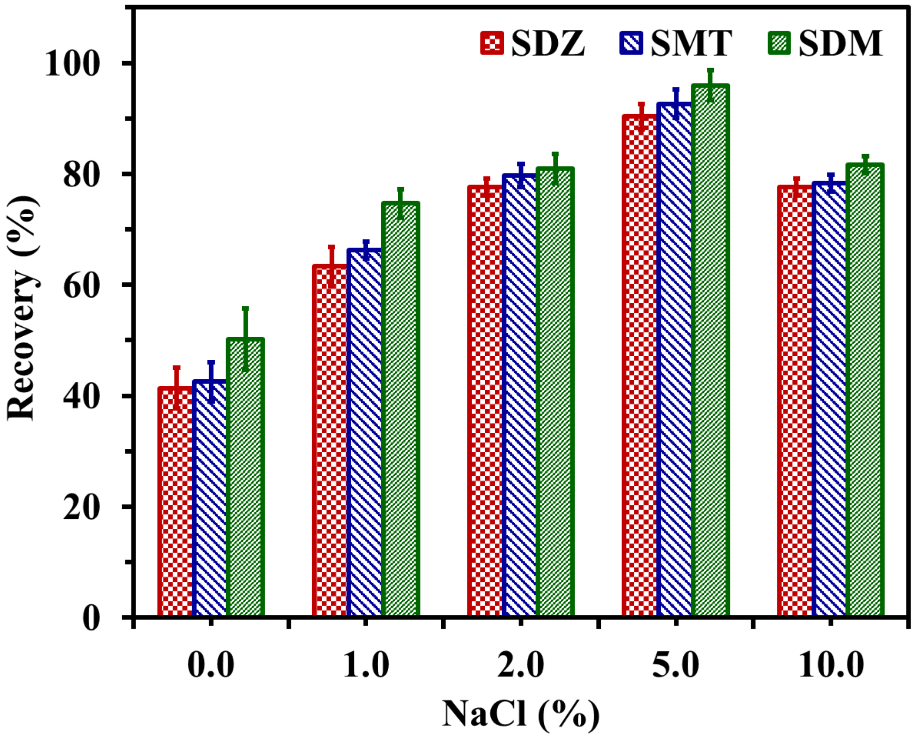

Fig. S10 Effect of sample solution ionic strength (NaCl) on the extraction of sulfonamides using the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

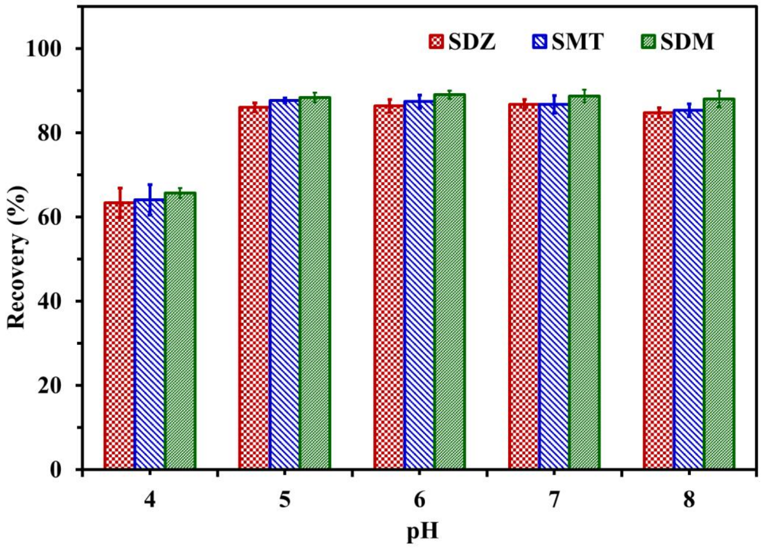

Fig. S11 Effect of sample pH on the extraction efficiency of sulfonamides with the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent (n=3).

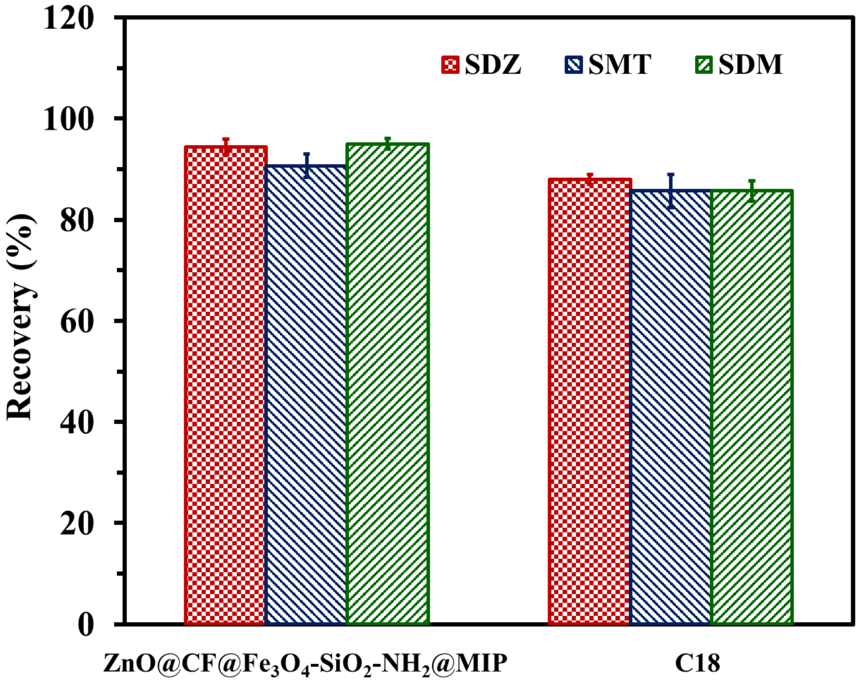

Fig. S12 Recoveries of sulfonamides using the proposed hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP and a C18 adsorbent (n=3).

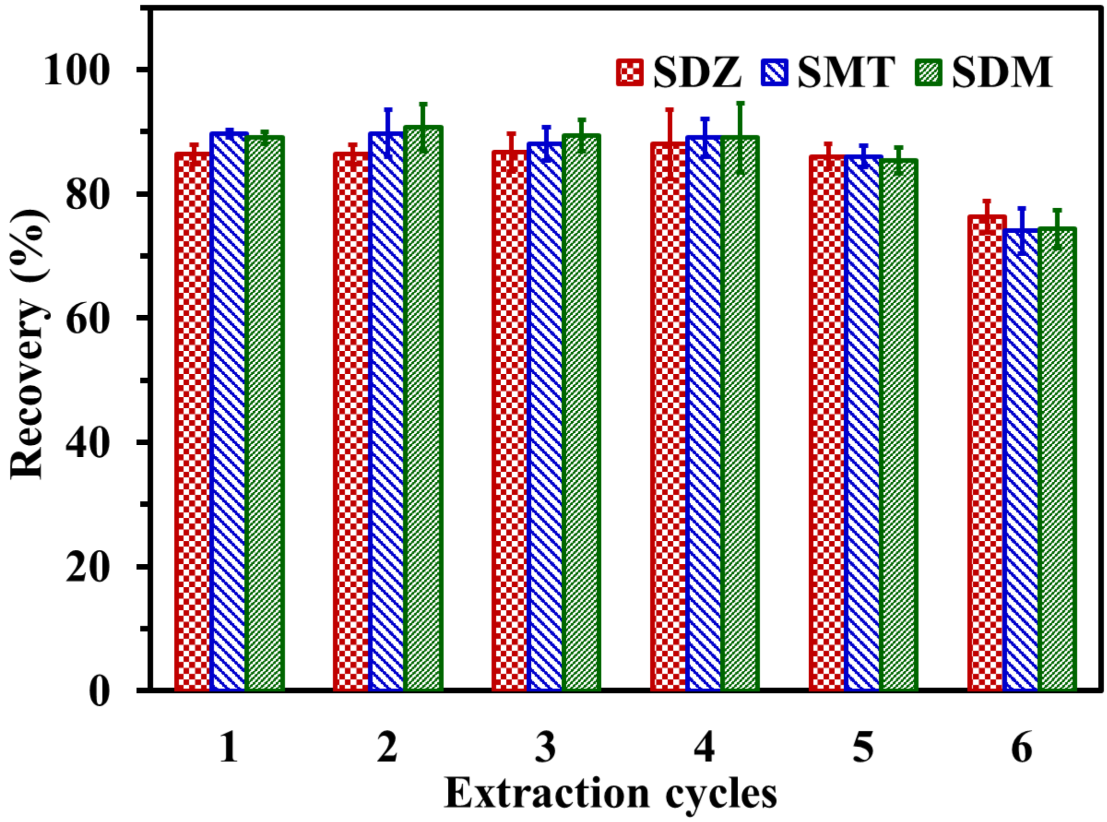

Fig. S13 The stability of the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent for the extraction and determination of sulfonamides (n=3).

Table S1 The linear regression of the pseudo-first-order and pseudo-second-order models for the adsorption of three target sulfonamides on the hierarchical nanocomposite ZnO@CF@Fe_3O_4-SiO_2-NH_2@MIP adsorbent

Analyte	Coefficient of determination (R^2)	
	Pseudo-first-order	Pseudo-second-order
SDZ	0.0393	0.9999
SMT	0.0100	0.9991
SDM	0.0079	0.9992

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