Development of Porous Composite Adsorbents for the Extraction and Determination of Trace Organic Compounds in Foods and Personal Care Products

Pattamaporn Klongklaew

A Thesis Submitted in Partial Fulfillment of the Requirements for the
Degree of Doctor of Philosophy in Chemistry (International Program)
Prince of Songkla University
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Author	Miss Pattamaporn Klongklaew
Major Program	Chemistry (International Program)

Major Advisor	**Examining Committee:**
……………………………………… (Assoc. Prof. Dr. Opas Bunkoed)	……………………………..Chairperson (Dr. Piyaluk Nurerk)
Co-Advisor	………………………………Committee (Assoc. Prof. Dr. Opas Bunkoed)
…………………………….............. (Assoc. Prof. Dr. Proespichaya Kanatharana)	……………………………...Committee (Assoc. Prof. Dr. Warakorn Limbut)
	……………………………...Committee (Assoc. Prof. Dr. Pongsaton Amornpitoksuk)
	…………………...……….Committee (Asst. Prof. Dr. Apichai Phonchai)
	…………………...……….Committee (Dr. Panwadee Wattanasin)

The Graduate School, Prince of Songkla University, has approved this thesis as partial fulfillment of the requirements for the Doctor of Philosophy Degree in Chemistry

………………………………………
(Prof. Dr. Damrongsak Faroongsarng)
Dean of Graduate School

This is to certify that the work here submitted is the result of the candidate's own investigations. Due acknowledgement has been made of any assistance received.

……………..………..……….Signature
(Assoc. Prof. Dr. Opas Bunkoed)
Major Advisor

……………..………..……….Signature
(Miss Pattamaporn Klongklaew)
Candidate

I hereby certify that this work has not been accepted in substance for any degree, and is not being currently submitted in candidature for any degree.

……...………....……….Signature
(Miss Pattamaporn Klongklaew)
Candidate

ชื่อวิทยานิพนธ์	การพัฒนาตัวดูดซับคอมโพสิทชนิดที่มีรูพรุน สำหรับสกัดและตรวจวิเคราะห์สารอินทรีย์ปริมาณน้อยในตัวอย่างอาหารและผลิตภัณฑ์ดูแลความสะอาด
ผู้เขียน	นางสาวปัทมาภรณ์ คล่องแคล่ว
สาขาวิชา	เคมี
ปีการศึกษา	2564

บทคัดย่อ

วิทยานิพนธ์นี้มีวัตถุประสงค์เพื่อพัฒนาตัวดูดซับคอมโพสิทชนิดที่มีรูพรุนสำหรับการสกัดเพิ่มความเข้มข้นและตรวจวิเคราะห์สารประกอบอินทรีย์ปริมาณน้อยในตัวอย่างอาหารและผลิตภัณฑ์ดูแลความสะอาดก่อนการวิเคราะห์ด้วยเครื่องมือทางด้านโครมาโทกราฟี โดยแบ่งออกเป็น 3 งานวิจัยย่อยตามชนิดของตัวดูดซับ ขั้นตอนการสกัด และชนิดของสารอินทรีย์ที่ตรวจวิเคราะห์

ในงานวิจัยแรกเป็นการพัฒนาตัวดูดซับโมโนลิทชนิดที่มีรูพรุนสูงประกอบด้วยพอลิไพโรลคอมโพสิทร่วมกับออกตะเดซิลที่เคลือบผิวซิลิกาและแกรฟีนออกไซด์ที่กักอยู่ในไคโตซานครัยโอเจล โดยนำตัวดูดซับดังกล่าวมาใช้สกัดยาฆ่าแมลงกลุ่มคาร์บาเมต 4 ชนิด ได้แก่ คาร์โบฟูแรน คาร์บาริล ไอโซโพรคาร์บ และไดโทเฟนคาร์บที่ตกค้างในตัวอย่างน้ำผลไม้ โดยไคโตซานครัยโอเจลมีลักษณะโครงสร้างที่มีรูพรุนคล้ายฟองน้ำ ช่วยให้สามารถลดแรงดันต้านกลับของตัวดูดซับในคาร์ทริดจ์ และช่วยเพิ่มพื้นที่ในการจับกับวัสดุคอมโพสิทบนพื้นผิว หรือภายในรูพรุนของไคโตซาน นอกจากนี้พอลิไพโรล ออกตะเดซิลและแกรฟีนออกไซด์สามารถดูดซับสารกลุ่มคาร์บาเมตได้ด้วยอันตรกิริยาแบบไฮโดรโฟบิค อันตรกิริยาแบบ π-π และพันธะไฮโดรเจน ภายใต้สภาวะที่เหมาะสมของเทคนิคโครมาโทกราฟีของเหลวสมรรถนะสูงและขั้นตอนการสกัดด้วยตัวดูดซับที่พัฒนาขึ้นพบว่าให้ช่วงความเป็นเส้นตรงตั้งแต่ 2 ถึง 500 ไมโครกรัมต่อลิตรสำหรับไอโซโพรคาร์บ 1 ถึง 500 ไมโครกรัมต่อลิตรสำหรับไดโทเฟนคาร์บและคาร์โบฟูแรน และ 0.5 ถึง 500 ไมโครกรัมต่อลิตรสำหรับคาร์บาริล มีขีดจำกัดการตรวจวัดอยู่ในช่วง 0.5 ถึง 2 ไมโครกรัมต่อลิตร ได้ประยุกต์ใช้วิธีที่พัฒนาขึ้นในการสกัดยาฆ่าแมลงกลุ่มคาร์บาเมตทั้ง 4 ชนิดในตัวอย่างน้ำแอปเปิ้ล องุ่น ส้ม มะเขือเทศ และน้ำทับทิม ซึ่งให้ค่าร้อยละการได้กลับคืนที่ดีในช่วง 84 ถึง 99 และค่าร้อยละเบี่ยงแบนมาตรฐานน้อยกว่า 6 นอกจากนี้ตัวดูดซับที่พัฒนาขึ้นมีเสถียรภาพที่ดี โดยสามารถนำกลับมาใช้ในการสกัดซ้ำได้ถึง 13 ครั้ง

งานวิจัยที่ 2 เป็นการพัฒนาตัวดูดซับคอมโพสิทพอลีอะนิลีน แกรฟีนออกไซด์และอนุภาคแม่เหล็กเคลือบด้วยออกตะเดซิลซิลิกาที่กักอยู่ในเม็ดอัลจิเนตชนิดที่มีรูพรุนสองชั้น สำหรับสกัดและเพิ่มความเข้มข้นสารกลุ่มฟลูออโรควิโนโลน โดยพอลีอะนิลีนและแกรฟีนออกไซด์สามารถดูดซับสารกลุ่มฟลูออโรควิโนโลนได้ด้วยพันธะไฮโดรเจน และอันตรกิริยาแบบ π-π ในขณะที่ออกตะเดซิลสามารถดูดซับสารที่ต้องการวิเคราะห์ได้ด้วยอันตรกิริยาแบบไฮโดรโฟบิค ลักษณะโครงสร้างที่มีรูพรุนสองชั้นของอัลจิเนตไฮโดรเจลเกิดจากปฏิกิริยาระหว่างแคลเซียมคาร์บอเนตและกรดไฮโดรคลอริค ซึ่งช่วยเพิ่มพื้นที่ผิวในการเคลือบพอลีอะนิลีน ทำให้สามารถดูดซับสารกลุ่มฟลูออโรควิโนโลนบนตัวดูดซับที่พัฒนาได้ดีขึ้น นอกจากนี้อนุภาคแม่เหล็กที่กักอยู่ในเม็ดอัลจิเนต ช่วยให้แยกตัวดูดซับออกจากสารตัวอย่างได้ง่ายและรวดเร็ว ด้วยการใช้แท่งแม่เหล็กภายนอก ภายใต้สภาวะที่เหมาะสมพบว่าวิธีที่พัฒนาขึ้นให้ขีดจำกัดการตรวจวัดอยู่ในช่วง 0.001 ถึง 0.01 ไมโครกรัมต่อลิตร ให้ช่วงความเป็นเส้นตรงตั้งแต่ 0.01 ถึง 50 ไมโครกรัมต่อลิตรสำหรับไดฟลอคซาซินและซาราฟลอคซาซิน 0.005 ถึง 50 ไมโครกรัมต่อลิตรสำหรับไซโปรฟลอคซาซิน เอนโรฟลอคซาซินและนอร์ฟลอคซาซิน และ 0.001 ถึง 50 ไมโครกรัมต่อลิตรสำหรับดาโนฟลอคซาซิน ได้ประยุกต์ใช้ตัวดูดซับที่พัฒนาขึ้นในการสกัดสารกลุ่มฟลูออโรควิโนโลนในตัวอย่างไข่ น้ำผึ้ง และนม โดยให้ค่าร้อยละการได้กลับคืนที่ยอมรับได้อยู่ในช่วง 81 ถึง 98 มีค่าการทำซ้ำและการใช้ซ้ำที่ดี โดยให้ค่าร้อยละเบี่ยงแบนมาตรฐาน น้อยกว่า 9 และสามารถนำกลับมาใช้ซ้ำได้ 7 ครั้ง

งานวิจัยที่ 3 เป็นการพัฒนาตัวดูดซับคอมโพสิทวัสดุโครงข่ายโลหะอินทรีย์และอนุภาคแม่เหล็กที่กักอยู่ในเม็ดคาราจีแนน แล้วเคลือบด้วยพอลีโดพามีนสำหรับสกัดสารกลุ่มพาราเบน โดยคาราจีแนนถูกนำมาใช้ในงานวิจัยนี้เนื่องจากมีข้อดีคือ มีความเป็นพิษต่ำ ย่อยสลายได้ง่าย และสามารถนำมาใช้ในการทำเป็นวัสดุคอมโพสิทร่วมกับอนุภาคแม่เหล็กได้ง่าย ซึ่งวัสดุโครงข่ายโลหะอินทรีย์และพอลีโดพามีนสามารถดูดซับสารกลุ่มพาราเบนได้ด้วยอันตรกิริยาแบบไฮโดรโฟบิค พันธะไฮโดรเจนและอันตรกิริยาแบบ π-π เมื่อศึกษาปัจจัยที่ส่งผลต่อการสกัดพบว่าภายใต้สภาวะที่เหมาะสม ตัวดูดซับที่พัฒนาขึ้นให้ขีดจำกัดการตรวจวัดตั้งแต่ 0.05 ถึง 1 ไมโครกรัมต่อลิตร มีช่วงความเป็นเส้นตรงในช่วงกว้างตั้งแต่ 2 ถึง 100 ไมโครกรัมต่อลิตรสำหรับบิวทิลพาราเบนและโพรพิลพาราเบน 0.05 ถึง 100 ไมโครกรัมต่อลิตรสำหรับเอทิลพาราเบน และ 0.01 ถึง 100 ไมโครกรัมต่อลิตรสำหรับเมทิลพาราเบน เมื่อนำตัวดูดซับที่พัฒนาขึ้นไปประยุกต์ใช้ในการสกัดสารกลุ่มพาราเบนในตัวอย่างน้ำยาบ้วนปากและผลิตภัณฑ์ทำความสะอาดผิวพบว่าให้ค่าร้อยละการได้

กลับคืนอยู่ในช่วง 80 ถึง 96 โดยมีร้อยละเบี่ยงแบนมาตรฐานน้อยกว่า 7 และมีค่าความเสถียรทางกายภาพที่ดีทำให้สามารถนำกลับมาใช้ซ้ำได้ 6 ครั้ง

โดยสรุปผลของการศึกษาแสดงให้เห็นว่าตัวดูดซับคอมโพสิทชนิดที่มีรูพรุนที่พัฒนาขึ้นสำหรับเทคนิคการเตรียมตัวอย่างก่อนการวิเคราะห์ด้วยเครื่องมือ สามารถนำมาใช้ในการสกัดเพิ่มความเข้มข้นและตรวจวิเคราะห์สารประกอบอินทรีย์ปริมาณน้อยในตัวอย่างอาหารและผลิตภัณฑ์ดูแลความสะอาดได้ โดยตัวดูดซับที่พัฒนาขึ้นมีประสิทธิภาพในการสกัดสูง มีความสามารถในการใช้ซ้ำและการทำซ้ำที่ดี นอกจากนี้ยังสามารถใช้งานได้ง่าย มีขั้นตอนการเตรียมที่ไม่ซับซ้อน เป็นมิตรกับสิ่งแวดล้อม และสามารถนำไปประยุกต์ใช้สำหรับสกัดสารประกอบอินทรีย์ชนิดอื่นที่สามารถเกิดอันตรกิริยากับตัวดูดซับที่พัฒนาขึ้นด้วยพันธะไฮโดรเจน อันตรกิริยาแบบ **π-π** และอันตรกิริยาแบบไฮโดรโฟบิคได้ โดยการปรับเปลี่ยนสภาวะให้เหมาะสมกับสารที่ต้องการวิเคราะห์

Thesis Title	Development of Porous Composite Adsorbents for the Extraction and Determination of Trace Organic Compounds in Foods and Personal Care Products
Major Program	Chemistry
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Abstract

This thesis aimed to develop porous composite adsorbents for the extraction, enrichment and determination of trace organic compounds in foods and personal care products before analysis with chromatographic technique. This thesis consists of three sub-projects divided by type of the adsorbent, extraction process and target analytes.

In the first sub-project, the high porous monolith adsorbent of polypyrrole composite octadecyl silica and graphene oxide embedded in chitosan cryogel (PPY/C18/GOx/Chi) was successfully developed and utilized as SPE sorbent for the extraction of four carbamate pesticides including carbofuran, carbaryl, isoprocarb, and diethofencarb in fruit juices. The sponge-like structure of chitosan cryogel adsorbent not only can reduce back pressure in SPE cartridge but also can improve the adsorption site of the adsorbent that help to entrap other composite materials into the pore or its surface. The composite materials of polypyrrole, octadecyl and graphene oxide can adsorb carbamate pesticides via hydrophobic interaction, π-π interaction and hydrogen bonding. Under the optimum conditions of HPLC system and the extraction process, the porous composite monolith adsorbent exhibited wide linear responses from 2 to 500 µg L^{-1} for isoprocarb, 1 to 500 µg L^{-1} for diethofencarb and carbofuran and 0.5 to 500 µg L^{-1} for carbaryl. The limit of detections (LODs) were in the range of 0.5 to 2 µg L^{-1}. The recovery of PPY/C18/GOx chitosan cryogel adsorbent when applied to extract four carbamate pesticides in apple, grape, orange, tomato and pomegranate juices were achieved from 84 to 99% with relative standard deviations (RSDs) lower than 6%. Moreover, it was great stability which can be reused up to 13 extraction cycles.

For the second sub-project, the doubly porous composite of polyaniline, octadecyl-bonded silica magnetite nanoparticles and graphene oxide incorporated in alginate beads (PANI/C18@SiO_2@Fe_3O_4/GOx) was fabricated and employed as magnetic solid phase extraction adsorbent (MSPE) for the extraction, enrichment and determination of fluoroquinolones. Polyaniline and graphene oxide can adsorb target fluoroquinolones via hydrogen bonding and π-π interaction and C18 can adsorb target fluoroquinolones via hydrophobic interaction. The double porous structure of alginate hydrogel was established by the reaction between calcium carbonate and hydrochloric acid. It can help to enhance the surface area for polyaniline coating which provided high adsorption site to adsorb fluoroquinolones. The magnetic nanoparticles in alginate beads promoted convenient and rapid separate the adsorbent from sample solution by applying only an external magnet. Under the optimal condition, the doubly porous alginate adsorbent provided low limit of detection from 0.001 to 0.01 µg L^{-1}. The linearity of PANI/C18@SiO_2@Fe_3O_4/GOx/Algi adsorbent were obtained in the range of 0.01 to 50 µg L^{-1} for difloxacin and sarafloxacin, 0.005 to 50 µg L^{-1} for ciprofloxacin, enrofloxacin and norfloxacin and 0.001 to 50 µg L^{-1} for danofloxacin. When the PANI/C18@SiO_2@Fe_3O_4/GOx/Algi adsorbent was applied to extract and pretreat fluoroquinolones in eggs, honey and milk samples, the satisfactory recoveries were acquired from 81 to 98%. It also provided good reproducibility with the RSDs less than 9% and good reusability which can be used to extract the target fluoroquinolones up to 7 times.

The third sub-project was the polydopamine coated porous composite materials of metal organic framework and Fe_3O_4 nanoparticles incorporated in carrageenan beads (PDA/MIL-101/Fe_3O_4/Carr) for the extraction of parabens. Carrageenan hydrogel was utilized as biodegradable and non-toxic supporting material which can easily entrap the composite materials and Fe_3O_4 nanoparticles. Metal organic frameworks type MIL-101(Cr) and polydopamine were used as the main composite materials to interact with four target parabens via hydrophobic interaction, hydrogen bonding and π-π interaction. Various affecting factors were investigated and optimized to obtain the best extraction efficiency. The results of PDA/MIL-101/Fe_3O_4/Carr adsorbent showed low limit of detections for all parabens from 0.05 to 1.0 µg L^{-1} and wide linear response in the range of 2 to 100 µg L^{-1} for butyl paraben and propyl paraben, 0.5 to 100 µg L^{-1} for ethyl paraben and 0.1 to 100 µg L^{-1} for methyl paraben. The good recoveries of the PDA/MIL-101/Fe_3O_4/Carr beads for parabens extraction in mouthwash and skin cleansers were achieved between 80 to 96% with relative standard deviations lower than 7%. It also had good physical stability which can be used for the extraction of parabens up to 6 cycles.

In the conclusion, the porous composite adsorbents were successfully fabricated and utilized for the extraction and enrichment of trace organic compounds in foods and personal care products before analysis with HPLC technique. These developed adsorbents exhibited high extraction efficiency, good reusability and reproducibility. There are several advantages including simple to prepare, convenient to use, environmentally and friendly. Moreover, the developed porous composite adsorbents can be applied for the extraction and determination of other organic compounds by modifying to achieve the suitable extraction condition with the target compounds.

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Pattamaporn Klongklaew

The Relevance of the Research Work to Thailand

The purpose of this Doctor of Philosophy Thesis in Chemistry is to develop and evaluate sample preparation techniques for the extraction, enrichment and determination of trace organic components in foods and personal care products. These developed adsorbents exhibited high extraction performance, simple to prepare, convenient to use, environmentally friendly and cost effective. They can be applied for the extraction of carbamate pesticides, fluoroquinolones and parabens in various samples including fruit juices, eggs, honey, milk, mouthwash and skin cleansers. Furthermore, they can be adapted as alternative method for the extraction of other organic contaminants at trace concentration levels which may be useful for any private sector and several government establishments in Thailand.

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List of abbreviations

Algi	Alginate
AOAC	Association of analytical communities
C18	Octadecyl
$CaCO_3$	Calcium carbonate
Carr	Carrageenan
Chi	Chitosan
CNS	Central nervous system
CO_2	Carbon dioxide
DAD	Diode array detector
DLLME	Dispersive liquid-liquid microextraction
Dt	2,5-dihydroxyterephthalaldehyde
d-SPME	Dispersive solid-phase microextraction
EC	European community
EU	European union
Fe_3O_4	Magnetic nanoparticles
FLD	Fluorescence detector
FQs	Fluoroquinolones
GOx	Graphene oxide
HCl	Hydrochloric acid
HPLC	High performance liquid chromatography
LLE	Liquid-liquid microextraction
LODs	Limit of detections
LOQs	Limit of quantifications
LPME	Liquid phase microextraction
MOFs	Metal organic frameworks
MRLs	Maximum residue limits
MSPE	Magnetic solid phase extraction
NOP	Nano-porous organic polymer
PAHs	Polycyclic aromatic hydrocarbons
PANI	Polyaniline

List of abbreviations

PDA	Polydopamine
ppb	Parts per billion
PPY	Polypyrrole
QuEChERS	Quick, easy, cheap, effective, rugged and safe
RSD	Relative standard deviation
SDME	Single drop microextraction
SBSE	Stir bar sorptive extraction
SiO_2	Silica
SPE	Solid phase extraction
SPME	Solid phase microextraction
Tb	1,3,5-tris(4-aminophenyl) benzene
US-EPA	United states environmental protection agency
UA-MSPE	Ultrasonic-assisted magnetic solid phase extraction
UV	Ultraviolet
ZIF-7	Zeolitic imidazolate framework

List of Publications

This thesis reported sample preparation techniques for the determination of trace organic compounds in foods and personal care products. Three sub-projects are included in this thesis. The following publications are referred using Roman numerals and attached in appendices at the end of thesis.

Paper I **Klongklaew, P.**, Naksena, T., Kanatharana, P., Bunkoed, O., A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices. ***Analytical and Bioanalytical Chemistry*** 410(27) (2018), 7185-7193.

Paper II **Klongklaew, P.**, Kanatharana, P., Bunkoed, O., Development of doubly porous composite adsorbent for the extraction of fluoroquinolones from food samples. ***Food Chemistry*** 309 (2020), 125685.

Paper III **Klongklaew, P.**, Bunkoed, O., The enrichment and extraction of parabens with polydopamine-coated microporous carrageenan hydrogel beads incorporating a hierarchical composite of metal-organic frameworks and magnetite nanoparticles. ***Microchemical Journal*** 165 (2021), 106103.

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Paper I

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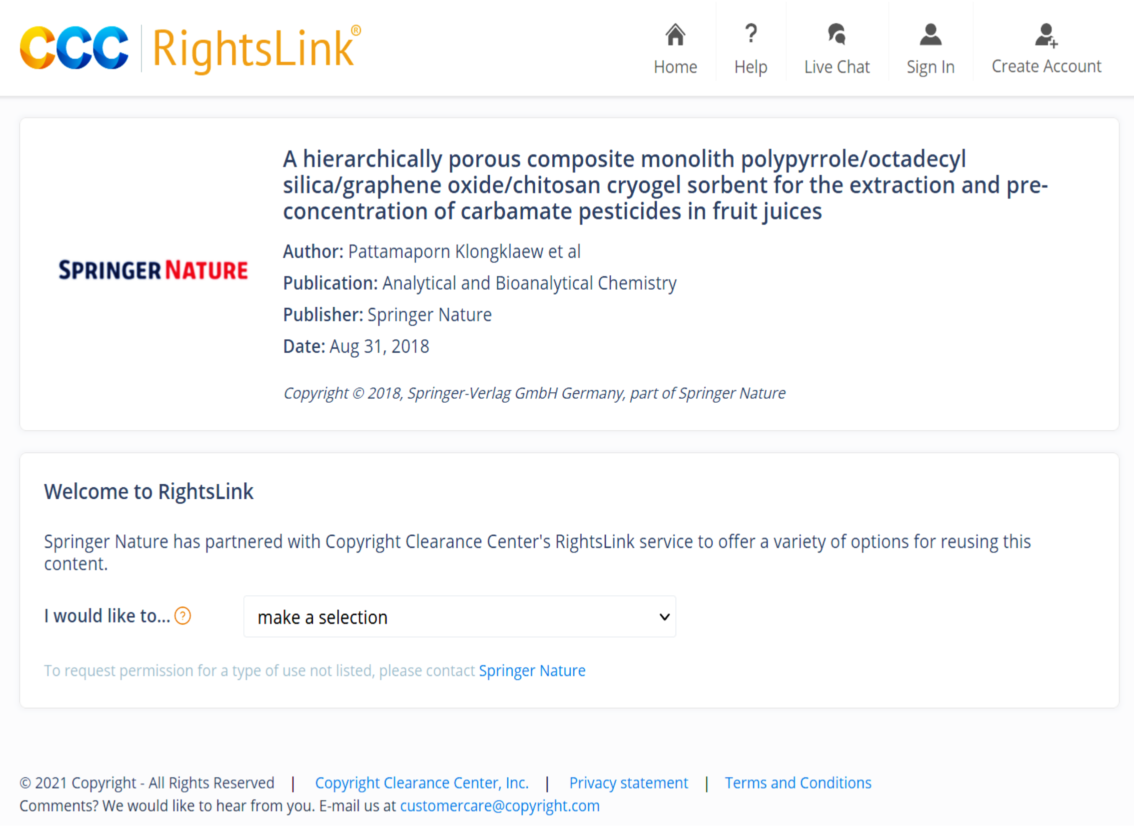

A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices

Author: Pattamaporn Klongklaew et al

Publication: Analytical and Bioanalytical Chemistry

Publisher: Springer Nature

Date: Aug 31, 2018

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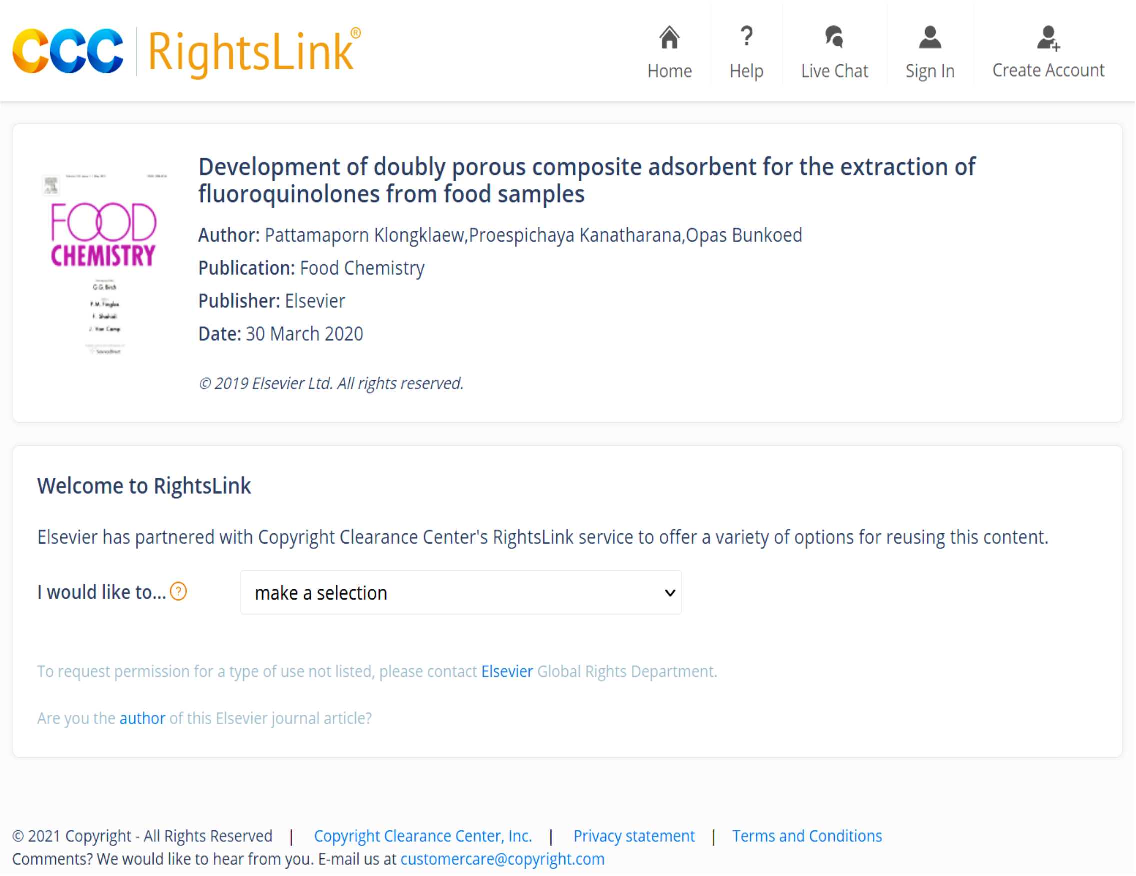

Development of doubly porous composite adsorbent for the extraction of fluoroquinolones from food samples

Author: Pattamaporn Klongklaew,Proespichaya Kanatharana,Opas Bunkoed

Publication: Food Chemistry

Publisher: Elsevier

Date: 30 March 2020

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Paper III

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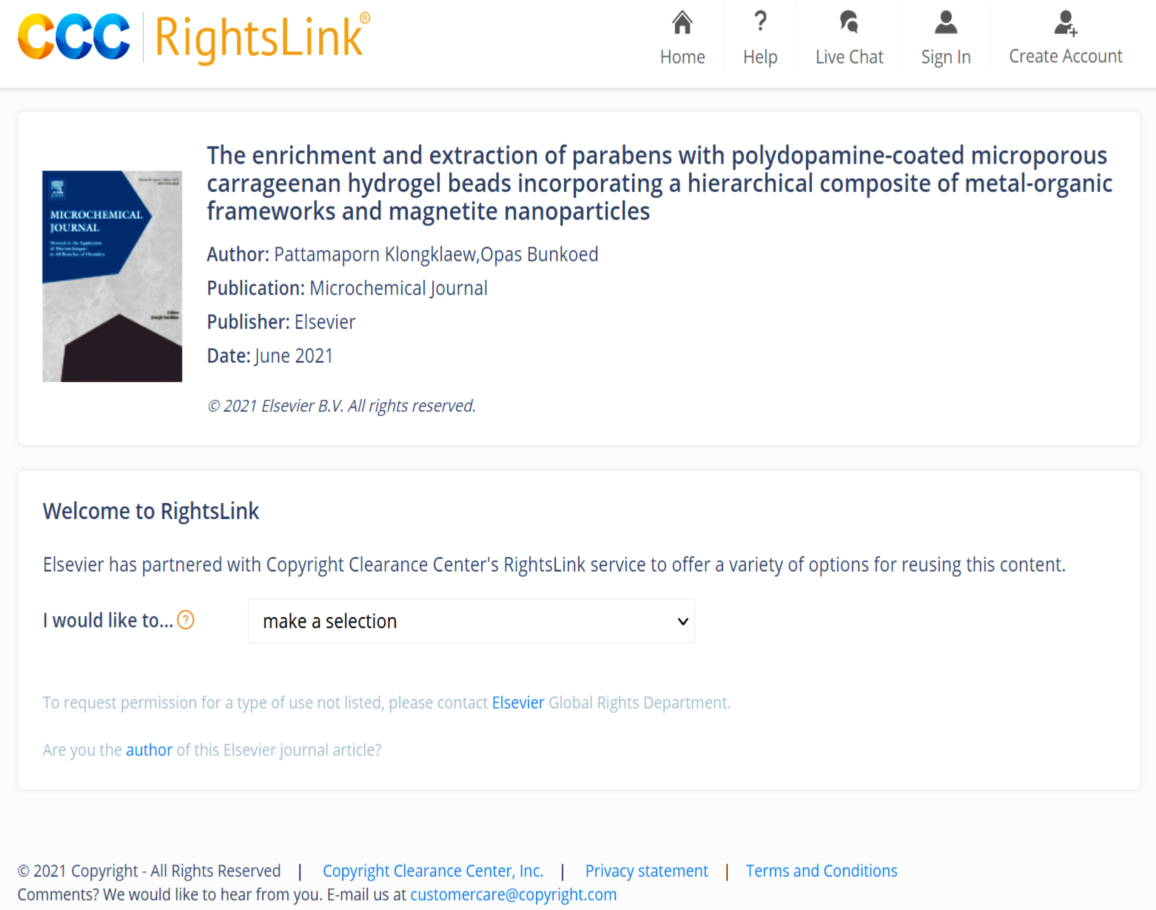

The enrichment and extraction of parabens with polydopamine-coated microporous carrageenan hydrogel beads incorporating a hierarchical composite of metal-organic frameworks and magnetite nanoparticles

Author: Pattamaporn Klongklaew,Opas Bunkoed

Publication: Microchemical Journal

Publisher: Elsevier

Date: June 2021

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1. Introduction

1.1 Background and rationale

Currently, various organic compounds such as insecticides, antibiotics and preservative compounds have abundant utilized in several field of agriculture and industry (Lu *et al.*, 2021; Molognoni *et al.*, 2019; Nalinci *et al.*, 2021). However, some specific properties of these organic compounds such as good stability, low biodegradability and poorly volatility can cause residues in environment, foods and agricultural products (da Cunha *et al.*, 2021; Guerra *et al.*, 2018; Yavir *et al.*, 2021). The primary effect of these compounds when enter into the food chain is associated with their ability to produce adverse human health effects (Abad-Gil *et al.*, 2021; Qiao *et al.*, 2021; Wang *et al.*, 2020).

Carbamate pesticides are insecticides which widely used in agriculture protection to control insects and fungi due to their broad-spectrum properties, well-high effectively and approximately low cost (Bhatt *et al.*, 2021; Chullasat *et al.*, 2020). Their residue in foods have potential hazard effects to human health such as headache, vomiting, uncontrolled urination or defecation and can cause carcinogenic to human (Changsan *et al.*, 2021; Wang *et al.*, 2019). Therefore, the United States Environmental Protection Agency (US-EPA) has set some carbamate pesticides as possibly carcinogenic to humans (EPA, 2002).

Fluoroquinolones (FQs) are synthetic antibiotics which widely used for human and veterinary medicines due to their high oral absorption rate, broad antibacterial activity and tissue penetration rates. They are often used for therapeutic purposes and as feed additives to promote livestock growth (Bagheri *et al.*, 2021; Li *et al.*, 2021; Mogolodi Dimpe *et al.*, 2019). Fluoroquinolones may also enter into the food chain due to their persist in edible tissue or foodstuff, not fully metabolized and low biodegradability in the body. In addition, the side effect of fluoroquinolones included disturbances in the central nervous system (CNS) and gastrointestinal tract, allergic reactions, tendon disorders and hepatotoxicity (Ashiq *et al.*, 2021; Wen *et al.*, 2020; Zhao *et al.*, 2021). To protect consumer health, the European Union (EU) has announced the maximum residue limits (MRLs) for fluoroquinolones in different tissue such as 10 µg kg^{-1} of sarafloxacin in chicken muscles and 100 µg kg^{-1} of ciprofloxacin in milk or meat samples (EU, 2001).

Parabens are basic preservative compounds that often added into synthesis process of various industry such as foodstuffs, toiletries, personal care products, beverages and cosmetics due to the properties of large antimicrobial protection and worthiness price (Jiang *et al.*, 2021; Zhang *et al.*, 2021). Their excessive usage and good stability may cause accumulate in environment and agricultural products which can cause health problems of the customers. The potential probability risks of paraben are skin allergic reaction, annoy the endocrine body system and can produce the breast cancer disease (Ariffin *et al.*, 2019; Feng *et al.*, 2016). To prevent the possibility of diseases, the maximum allowed levels was eliminated by European Community (EC) at 8 g kg^{-1} of parabens in cosmetic products (EU, 2014).

Therefore, it is necessary to develop a simple, rapid, reliable and highly sensitive methods for the determination of carbamate pesticides, fluoroquinolones and parabens in foods and personal care products. High performance liquid chromatography (HPLC) coupled with various detectors include ultraviolet (UV) (Abdolmohammad-Zadeh *et al.*, 2020; Cheng *et al.*, 2021), diode array detector (DAD) (Han *et al.*, 2021; Wu *et al.*, 2021; Yuvali *et al.*, 2020) and fluorescence detector (FLD) (Pang *et al.*, 2019; Wang *et al.*, 2018) is normally used to determine trace organic compounds due to its high sensitivity, good precision and can simultaneously determine several compounds using separation column. However, the concentration of toxic organic compounds in real samples are generally present at trace levels and usually contaminated with other matrices. Thus, the suitable and reliable sample preparation methods are required prior to instrumental analysis.

For the analysis of carbamate pesticides, fluoroquinolones and parabens, several sample preparation techniques have been developed for the extraction, purification and enrichment including liquid-liquid microextraction (LLE) (Diuzheva *et al.*, 2019; Fernández *et al.*, 2021; Yu *et al.*, 2021), solid phase extraction (SPE) (de Oliveira *et al.*, 2016; Razavi *et al.*, 2019; Wang *et al.*, 2019), solid phase microextraction (SPME) (Tang *et al.*, 2017; Wang *et al.*, 2020; Yazdi *et al.*, 2018), magnetic solid phase extraction (MSPE) (Jalilian *et al.*, 2019; Li *et al.*, 2017; Zhang *et al.*, 2021), stir bar sorptive extraction (SBSE) (Fan *et al.*, 2015; Hu *et al.*, 2013; Ramírez *et al.*, 2011), dispersive liquid–liquid microextraction (DLLME) (Shen *et al.*, 2020; Szarka *et al.*, 2018; Yu *et al.*, 2020), liquid phase microextraction (LPME) (Durak *et al.*, 2020;

Dowlatshah *et al.*, 2021; Santigosa *et al.*, 2019), quick, easy, cheap, effective, rugged and safe extraction (QuEChERS) (Malvar *et al.*, 2020; Sousa *et al.*, 2021; Zhang *et al.*, 2019) and single drop microextraction (SDME) (Gao *et al.*, 2011; Chullasat *et al.*, 2020; Mafra *et al.*, 2019). Among these extraction techniques, SPE is widely used due to its convenience, easy operation and provides high extraction efficiency. However, conventional packed SPE cartridge has the limitation of high back pressure which cannot load the sample at high flow rate, cannot be reused and expensive (Rattanakunsong *et al.*, 2020). To overcome these limitations, development of a porous structured monolith SPE sorbent is an interesting material. Chitosan cryogel is a good choice to prepare porous monolith sorbent due to it has macro-porous structure like a sponge pores that approximately applied to entrap other nanomaterials in the pores or on the surfaces of chitosan cryogel (Baimenov *et al.*, 2020; Yin *et al.*, 2021). In addition, it has the gainful properties of good biodegradability, cost effectively and low toxicity (Makkliang *et al.*, 2017). To improve the extraction efficiency of the adsorbent, the adsorption materials with various properties are much attract attention to embed into supporting material of the adsorbents. The composite materials not only improve the interaction between analytes and the adsorbent but also can reduce the extraction time. In this regards the integrating of octadecyl bonded silica, graphene oxide nanoparticles and polymer-based materials such as polypyrrole was selected as composite materials for the extraction of carbamate pesticides because of its high surface adsorption site and good chemical stability (Treder *et al.*, 2021; Mehdinia *et al.*, 2020; Xiao *et al.*, 2019; Karthikeyan *et al.*, 2021). Considering to graphene oxide particles and polypyrrole structure, their consist of basic functional groups of carboxylic, epoxide, hydroxyl, aromatic ring and amino groups which can provide strong adsorption for target analytes by π-π interaction and hydrogen bonding (Eskandari *et al.*, 2021; Yang *et al.*, 2019). While, long hydrocarbon chain of octadecyl can produce hydrophobic interaction as showed in **Figure 1**.

Recently, magnetic solid phase extraction (MSPE) has attracted much attention to extract and pretreat the target analytes in various samples due to the separation process of the adsorbent from a sample solution can be performed using an external magnet, which makes the faster and easier separation and its can be reused after basic washing step with the suitable washing solution (Ding *et al.*, 2021; Gopal *et al.*, 2020).

Nevertheless, the bare magnetic nanoparticles (Fe_3O_4) are liable to aggregate, might oxidation at low pH and low selectivity. Thus, the surface of magnetic nanoparticles should be modified with specific ligands to improve the selectivity and dispersibility such as the octadecyl coated magnetite nanoparticle (C18-coated SiO_2@Fe_3O_4). To achieve rapid separation of nanoparticles and enhance the efficiency of adsorbent, the supporting materials and adsorption materials such as metal organic framework, graphene oxide and polymer-based materials of polyaniline and polydopamine are great necessary. Alginate and carrageenan were utilized as supporting materials to entrap the adsorption materials such as C18-coated SiO_2@Fe_3O_4 nanoparticles and graphene oxide in form of composite beads which would help to improve the dispersibility of the adsorbent in aqueous solution and easy to coat with the polymer. Metal organic framework is a class of high porous material that synthesized from hybrid organic-inorganic materials. It generally presented large structure cavities, uniform pattern and high chemical and thermal stability which can adsorb organic compounds via π-π interaction. While, polymer can interact with target analytes via π-π interaction and hydrogen bonding (Bagheri *et al.*, 2021; Duo *et al.*, 2020; Mukherjee *et al.*, 2021). The MSPE methods in this thesis consist of two hybrid composite adsorbents of the polyaniline composite graphene oxide and C18-coated SiO_2@Fe_3O_4 embedded in alginate beads (PANI/C18@SiO_2@Fe_3O_4/GOx/Algi) and the polydopamine, metal organic framework and Fe_3O_4 nanoparticles incorporated in carrageenan beads (PDA/MIL-101/Fe_3O_4/Carr). The major interaction of the PANI/C18@SiO_2@Fe_3O_4 /GOx alginate beads with fluoroquinolones and the PDA/MIL-101/Fe_3O_4 carrageenan beads with parabens are based on π-π, hydrophobic interaction and hydrogen bonding as shown in **Figure 2** and **3**, respectively.

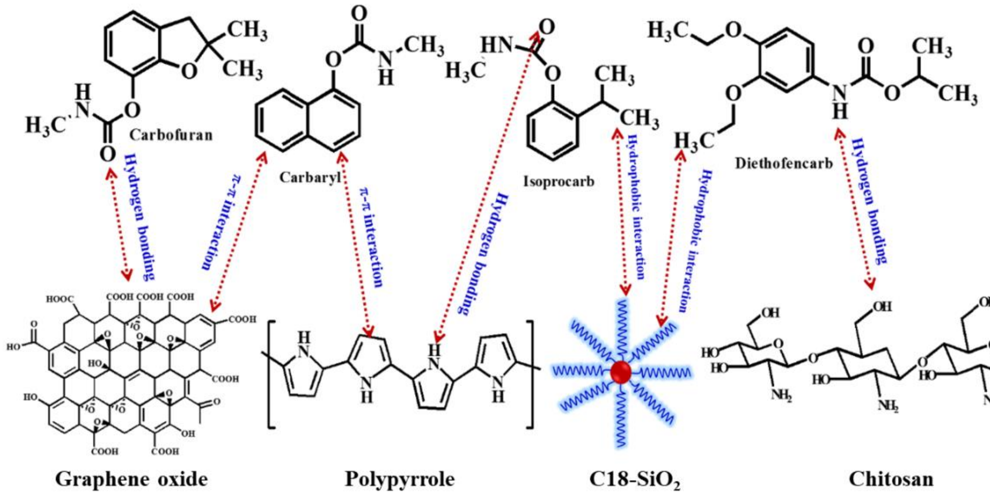


Figure 1 The interaction between the composite monolith PPY/C18/GOx chitosan cryogel adsorbent and carbamate pesticides

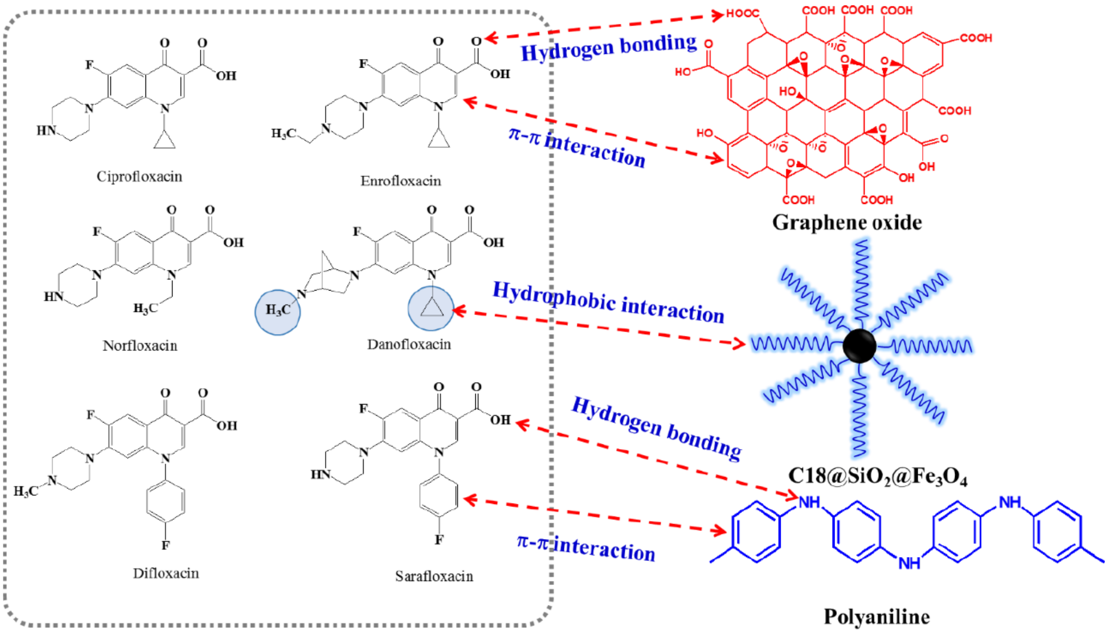


Figure 2 The interaction between the double porous micro-composite PANI/C18@SiO2@Fe3O4/GOx alginate hydrogel and fluoroquinolones

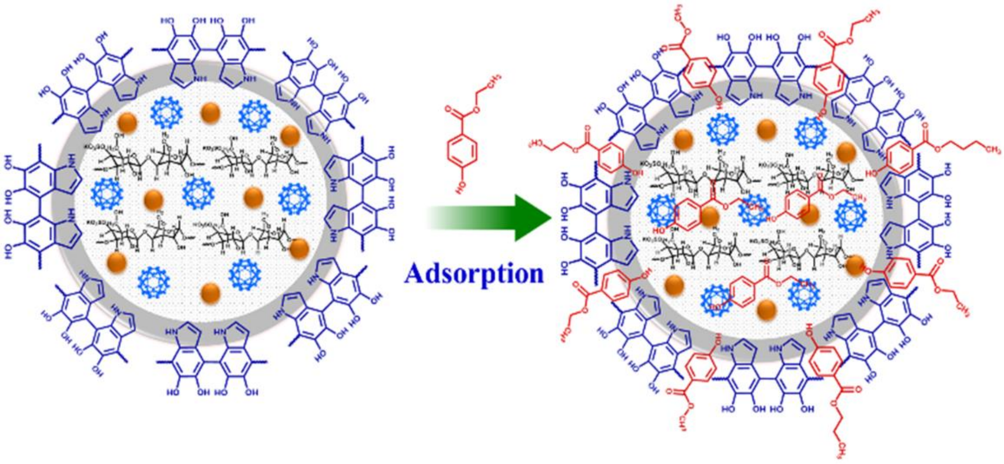


Figure 3 The interaction between parabens and the composite PDA/MIL-101/Fe_3O_4 carrageenan hydrogel adsorbent (Reprint from Klongklaew and coworker, 2021; copyright with permission from Elsevier) (Klongklaew *et al*., 2021)

1.2 Objective

The objective of this thesis is to develop sample preparation techniques for the extraction, enrichment and determination of trace organic compounds in foods and personal care products. To achieve this objective, three sub-projects were performed as follows:

Sub project I: The high porous monolith of polypyrrole composite octadecyl silica and graphene oxide embedded in chitosan cryogel (PPY/C18/GOx/Chi) adsorbent was developed and utilized in SPE technique for the extraction of carbamate pesticides in fruit juices.

Sub project II: The doubly porous composite of polyaniline, octadecyl-bonded silica magnetite nanoparticles and graphene oxide incorporated in alginate beads (PANI/C18@SiO_2@Fe_3O_4/GOx/Algi) was fabricated and employed as magnetic solid phase extraction adsorbent (MSPE) for the extraction and enrichment of fluoroquinolones in eggs, honey and milk samples.

Sub project III: The polydopamine coated porous composite materials between metal organic framework and Fe_3O_4 nanoparticles incorporated in carrageenan beads (PDA/MIL-101/Fe_3O_4/Carr) was fabricated for the extraction of parabens in mouthwash and skin cleansers.

2. Sample preparation techniques

Sample preparation technique is an important in analytical applications which is used to reduce sample size, pretreat the analytes and simplify matrix interferences before analysis with analytical instrument (Moldoveanu *et al.*, 2021; Li *et al.*, 2021). Recently, various sample preparation techniques were developed to obtain specific benefits of each application such as environmental analysis (Stock *et al.*, 2019), forensics (Hussain *et al.*, 2021), bioanalysis (Nazario *et al.*, 2017) and food analysis (Martins *et al.*, 2021). The developed methods are normally based on environmentally friendly, easy to synthesis, use less volume of toxic organic solvent and convenient to use in many analytical applications. The sample preparation techniques that have been reported for the determination of trace organic compounds including liquid-liquid extraction (LLE) (Tehranirokh *et al.*, 2021), solid phase extraction (SPE) (Maranata *et al.*, 2021), solid phase microextraction (SPME) (Lashgari *et al.*, 2019), magnetic solid phase extraction (MSPE) (Yin *et al.*, 2021), dispersive liquid-liquid microextraction (DLLME) (Heidarbeigi *et al.*, 2021), stir bar sorptive extraction (SBSE) (He *et al.*, 2021), quick, easy, cheap, effective, rugged and safe extraction (QuEChERS) (Hrynko *et al.*, 2021), single drop microextraction (SDME) (Kailasa *et al.*, 2021) and liquid phase microextraction (LPME) (Chormey *et al.*, 2020).

Among these sample preparation techniques, solid phase extraction and magnetic solid phase extraction methods are an interesting method for the extraction, purify and pre-concentration of trace organic compounds. These methods are easy to operate, convenient to use, used low amount of organic solvent and simple extraction process (Guo *et al.*, 2021; Pang *et al.*, 2021; Volynkin *et al.*, 2021; Wan *et al.*, 2021; Wang *et al.*, 2021).

2.1 Solid phase extraction

Solid phase extraction (SPE) is usually utilized as extractive sample preparation technique to separate the target analytes from other components or matrix inferences in aqueous samples by physical or chemical properties (Amiri *et al.*, 2021; Deflaoui *et al.*, 2021). The typical solid phase extraction procedure involves four basic steps as demonstrated in **Figure 4**. The first step is conditioning the solid adsorbent with the appropriate solution or organic solvent to remove some impurities on surface of the adsorbent. Next, aqueous solution or sample is loaded passthrough SPE cartridge with the constant flow rate. In this step, the target analytes interact with adsorption materials on the surface of adsorbents. Then, washing the adsorbent with intermediate strength of organic solution to eliminate some interferences in the samples. The last step is eluting. This step, the target analytes are eluted from the adsorbent with suitable organic solvent (Andrade-Eiroa *et al.*, 2016; Uflyand *et al.*, 2021). SPE method is widely used for the extraction and pre-concentration of various organic compounds in various samples as summarized in **Table 1**.

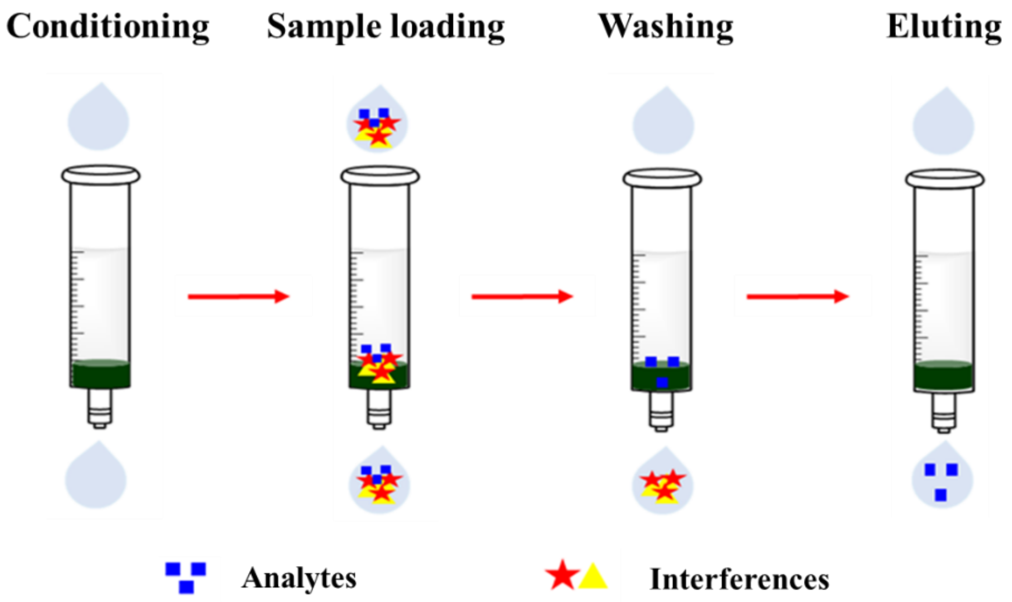


Figure 4 Solid phase extraction procedure

Table 1 Application of solid phase extraction technique for the extraction and pre-concentration of organic compounds

Analytes	Adsorbents	Sample	Sample volume (mL)	Recovery (%)	References
Aflatoxins	Silica/graphene oxide	Cereal crops	7.00	76.5-119	Yu *et al.*, 2018
Carbamate pesticides	Graphene	Water	50.0	81.1-111	Shi *et al.*, 2014
Carbamate pesticides	Porous organic polymer	Juice	100	82.0-110	Wang *et al.*, 2019
Fluoroquinolones	MIP	Human urine	0.250	87.5-96.4	de Oliveira *et al.*, 2016
Fluoroquinolones	MIP	Milk	1.00	76.8-97.7	Wang *et al.*, 2016
Nitroimidazoles	Triazine-based porous organic polymer	Honey and water	150	80.3-118	Goo *et al.*, 2021
Non-steroidal anti-inflammatory drugs	MOF-199 based sol-gel coated stainless steel mesh	Human plasma and water	50.0	93.6-99.6	Amiri *et al.*, 2021
Non-steroidal anti-inflammatory drugs	Poly (HEMA-co-EDMA)	Water	50.0	94.0-107	Medina *et al.*, 2020
Phenoxy carboxylic acids	MIL-101-ethylenediamine	Water	200	91.4-94.8	Deng *et al.*, 2021
Chlorophenols	Ferrocene-based NOP	Tap water, tea and juice	100	87.6-119	Wang *et al.*, 2019

2.2 Magnetic solid phase extraction

Magnetic solid phase extraction (MSPE) is a sample preparation technique based on functionalized magnetic materials. It generally operated in form of dispersive solid phase extraction which can improve the interfacial area of analytes and the adsorbent when compared with conventional SPE method (Grau *et al.*, 2021; Hassan *et al.*, 2021). The magnetic property of the adsorbent help to reduce the extraction time because it is easy and rapid to isolate the adsorbent from sample solution or organic solvent by applying the external magnet. The advantages of MSPE sorbent not only minimizes the sophisticated step of filtration or centrifugation in traditional methods but also can reuse the magnetic adsorbents with simple washing process (Mhd. Haniffa *et al.*, 2021). Therefore, the MSPE technique are widely used for the extraction and pre-concentration of trace organic compounds in different matrix interferences **(Table 2)**.

The magnetic extraction procedure has the main process of adsorption and desorption between target analytes and adsorbents as shown in **Figure 5**. Firstly, the magnetic adsorbents are added into aqueous solution and stir at appropriate rate with equilibrium time to completely adsorb target analytes. Next, the magnetic adsorbents are rapid and easy separated from aqueous solution using external magnet. Then, appropriate volume of suitable organic solvent or the mixture of acid and solvents were used to break the interaction of target analytes from the surface of the adsorbents. The eluent is evaporated until dryness at boiling point of organic solvent, reconstituted and filtrated through filter before simultaneously analysis with chromatography instrument (Amiri *et al.*, 2021).

Table 2 Applications of magnetic solid phase extraction technique for the extraction and pre-concentration of organic compounds

Analytes	Adsorbents	Sample	Sample volume (mL)	Recovery (%)	References
Fluoroquinolones	Fe_3O_4@Cys@MIL125-NH_2	Water	50.0	83.8-109	Lian *et al.*, 2018
Fluoroquinolones	Fe_3O_4@COF(TpBD)@Au-MPS	Meat	10.0	82.0-110	Wen *et al.*, 2020
Fluoroquinolones	Fe_3O_4@PDA@UPOPs	Milk, egg and chicken muscle	10.0	78.1-97.7	Li *et al.*, 2021
Organophosphorus pesticides	Magnetic chitosan/SiO_2/ZIF-67	Vegetable, fruit juice, and milk	10.0	83.7-98.1	Ghorbani *et al.*, 2021
Organophosphorus pesticides	PVA@MGO	Juice, and water	10.0	94.5-107	Nasiri *et al.*, 2021
Organophosphorus pesticides	Magnetic COF-Dt-Tb	Milk	5.00	80.0-105	Lin *et al.*, 2020
Organophosphorus pesticides	Fe_3O_4@COF@Zr^{4+}	Vegetables	10.0	87.0-121	Li *et al.*, 2021
Organophosphorus pesticides	Fe_3O_4@polyphenols	Vegetable, fruit and water	10.0	54.0-89.0	Yadeghari *et al.*, 2021

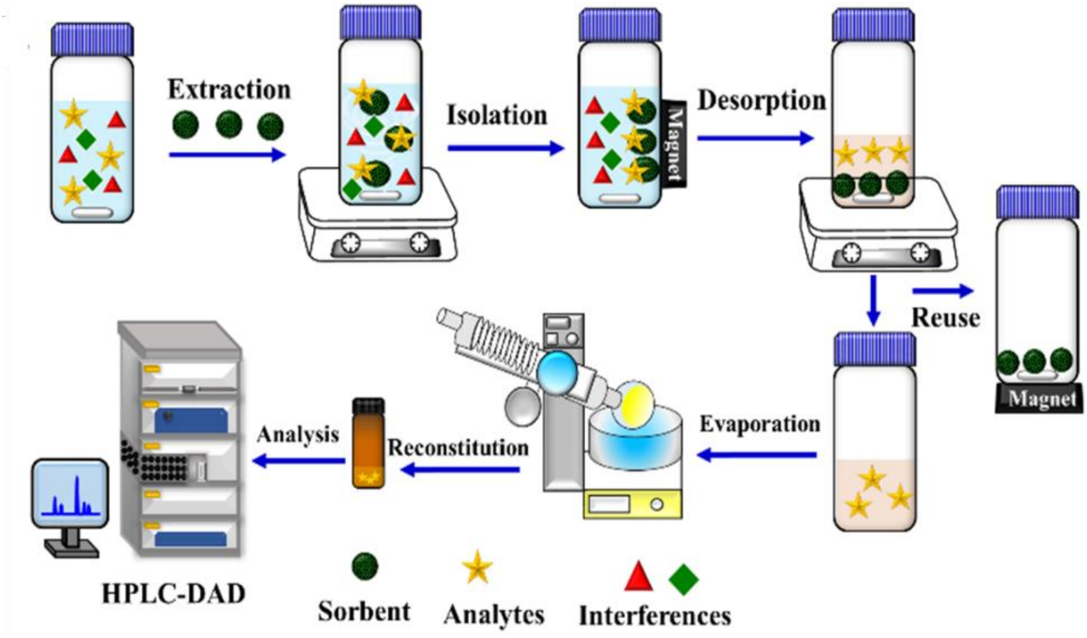


Figure 5 The extraction procedure of magnetic solid phase extraction (Reprint from Klongklaew and coworker, 2021; copyright with permission from Elsevier) (Klongklaew *et al.*, 2021)

3. Materials of the adsorbent

Materials of the adsorbent are referred to the compounds which have the special properties or functional groups to adsorb target analytes (Gil *et al.*, 2021; Liu *et al.*, 2020; Zhou *et al.*, 2019). This thesis consisted of two main types of adsorbent materials including supporting and adsorption materials.

3.1 Supporting materials

Supporting materials are used to embed other adsorption materials, increase porosity and help to improve dispersibility of the adsorbent in MSPE technique. The supporting materials should have some specific properties such as good thermal and physical stability, easily and rapidly cross-linking and high porosity (Glöckner *et al.*, 1987). The supporting materials in this thesis including chitosan cryogel, alginate and carrageenan hydrogel.

3.1.1 Chitosan cryogel

Chitosan is polysaccharide polymer that produced from deacetylation process of chitin. The advantage characteristics of chitosan are good biodegradability, chemical inertness and low toxicity. It generally consists of major functional groups of amino (-NH_2) and hydroxyl (-OH) in the molecular chains **(Figure 6A)** which provided high adsorption capacity. According to these reasons, chitosan is considerable attention to use as adsorbent materials in sample preparation techniques (Dragan *et al.*, 2019; Upadhyay *et al.*, 2021). To generate high porosity of the adsorbent, chitosan cryogel was simple fabricated using polymer cross-linked under semi-freezing condition that call "cryogelation" process **(Figure 6B)**. After the ice crystals were thawed at room temperature, macro-porous network of chitosan cryogel was achieved with sponge-like structure and high elasticity **(Figure 7)**. The high porous structure of chitosan cryogel can increase surface areas of the adsorbent which help to entrap the other adsorption materials and also prevent the adsorption materials loss during the extraction process. In addition, the high porous structure can eliminate the limitation of high backpressure in the solid phase extraction process (Baimenov *et al.*, 2020).

Figure 6 Chitosan structure (A) and cryogelation process of chitosan (B)

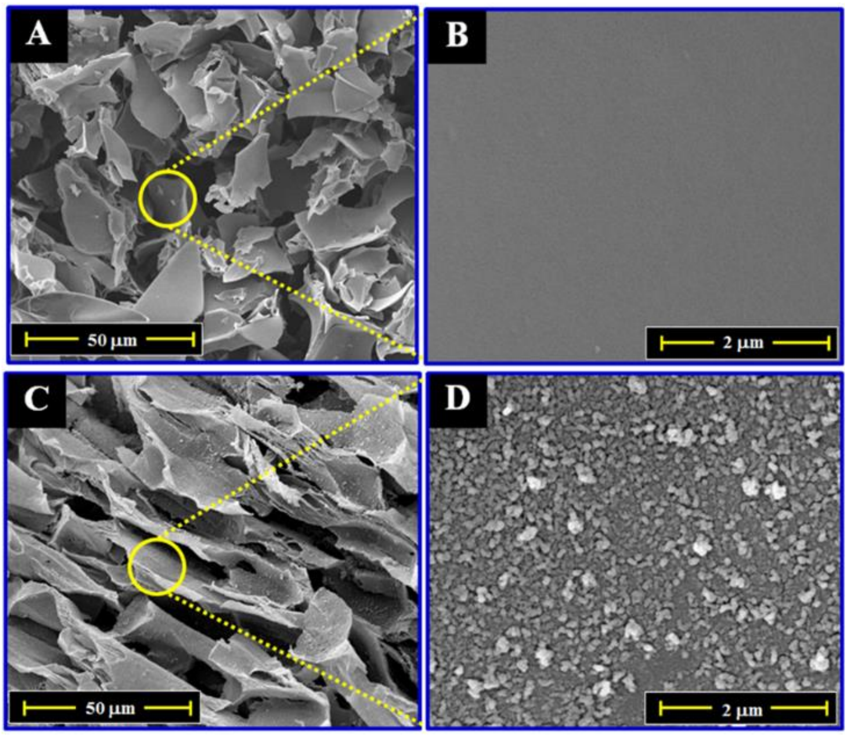


Figure 7 The SEM images of chitosan cryogel 1000X (A), 20000X (B) and composite of PPY/C18/GOx chitosan cryogel 1000X (C), 20000X (D) (Reprint from Klongklaew and coworker, 2018; copyright with permission from Springer Nature) (Klongklaew *et al.*, 2018)

3.1.2 Alginate hydrogel

Alginate is eatable water-soluble polysaccharide produced from cell wall of brown seaweed or algae which is environmentally friendly and good biodegradability material. Other interesting properties of alginate are easy to form stable network, like egg box structure, are anion exchange between alginic acid and divalent cations such as Ca^{2+} in safe and mild condition at room temperature **(Figure 8)** (Abasalizadeh *et al.*, 2020). Due to the structure of alginate generated from different sequence of 1→4 covalent linked between β-D-mannuronate and α-L-guluronate, the alginate gels are easily established with different pattern such as bead **(Figure 9A)** or fiber in high concentration of calcium chloride salt (Gao *et al.*, 2020; Sutirman *et al.*, 2021). The advantages of alginate hydrogel are high physical and thermal stability, rapidly form hydrogelation and suitable to entrap other adsorption materials such as hydrophobic materials, nanoparticles or large molecules (Iravani Mohammadabadi *et al.*, 2021;

Mokhtari *et al.*, 2021). To improve the porosity and surface areas of alginate beads, the doubly porous structure was fabricated from the reaction between calcium carbonate embedded inside alginate bead and hydrochloric acid (Zhuang *et al*, 2017). This reaction provided carbon dioxide bubble inside the bead which made double porous structure **(Figure 9B)** according to following equation:

$$CaCO_{3(s)} + 2HCl_{(aq)} \rightarrow CaCl_{2(aq)} + CO_{2(g)} + H_2O$$

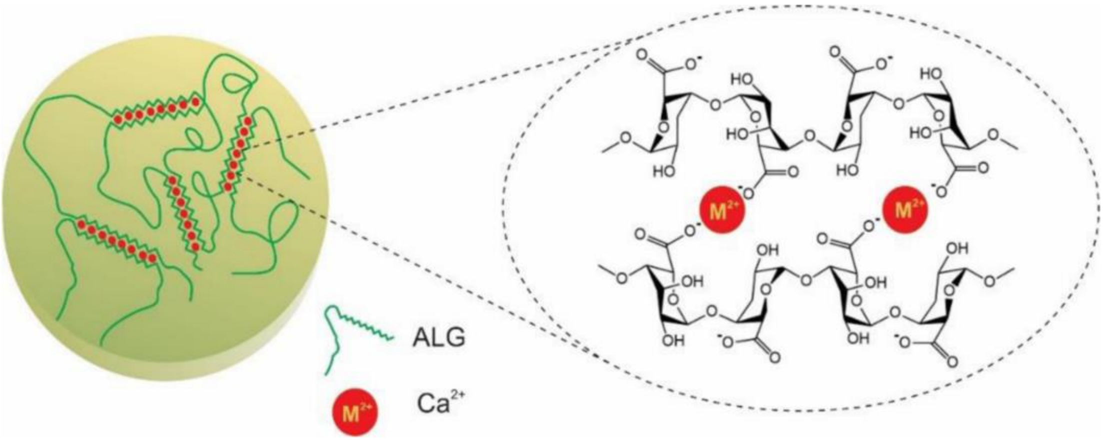


Figure 8 Egg-box structure for alginate gelation as a result of ionic interaction between alginate and a divalent cation (Reprint from Abasalizadeh and coworker, 2020; copyright with permission from Springer) (Abasalizadeh *et al.*, 2020)

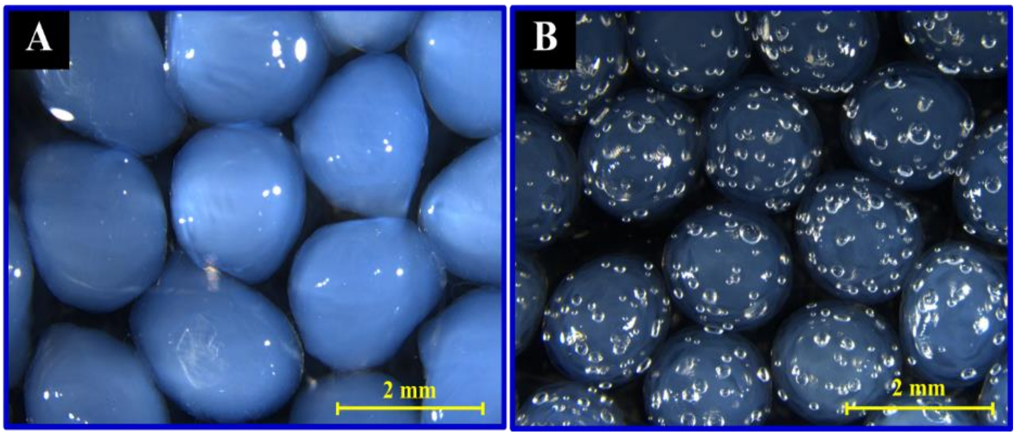


Figure 9 Photograph of microcomposite alginate hydrogel (A) and double porous microcomposite hydrogel (B) (Reprint from Klongklaew and coworker, 2020; copyright with permission from Elsevier) (Klongklaew *et al.*, 2020)

3.1.3 Carrageenan hydrogel

Carrageenan is sulfated anionic polysaccharides biopolymer which generally produced from red seaweed. It basically consists of alternative linked blocks of β-d-galactose and α-d-galactose or 3,6-anhydro-α-d-galactose which provided kappa (κ), iota (ι), and lambda (λ) types of carrageenan depended on algae type and synthesis method (dos Santos *et al*, 2015). Recently, κ-carrageenan has received much great attention due to its non-toxicity, thermal reversibility, high adsorption capacity and easy gelling. The special hydrogelation processes of carrageenan are based on both of temperature and gel inducing agent to form stable three-dimensional structure of aggregation helical dimers **(Figure 10)** (Rhein-Knudsen, *et al.*, 2015). Therefore, carrageenan hydrogel is mostly performed by ionic cross linker between sulfated of carrageenan structure and potassium ions (K^+) (Kulal, *et al.*, 2020; Pishnamazi, *et al.*, 2020). The form of carrageenan bead is mostly used to synthesize the adsorbent because it is suitable to disperse in sample solution, simple to entrap the adsorption materials and prevent the loss of adsorption materials from hydrogel adsorbent (Duman *et al.*, 2019; Sebeia *et al.*, 2019).

Chitosan cryogel, alginate and carrageenan hydrogel have been widely used as supporting materials in various applications **(Table 3)**. In this thesis, chitosan was used for solid phase extraction because it has broad spectrum properties, provided large porous structure which can reduce backpressure of SPE cartridge and suitable to form monolith sorbent. While, alginate and carrageenan were used for magnetic solid phase extraction adsorbent due to they can be easily synthesized in bead form and can entrap various adsorption materials inside the bead.

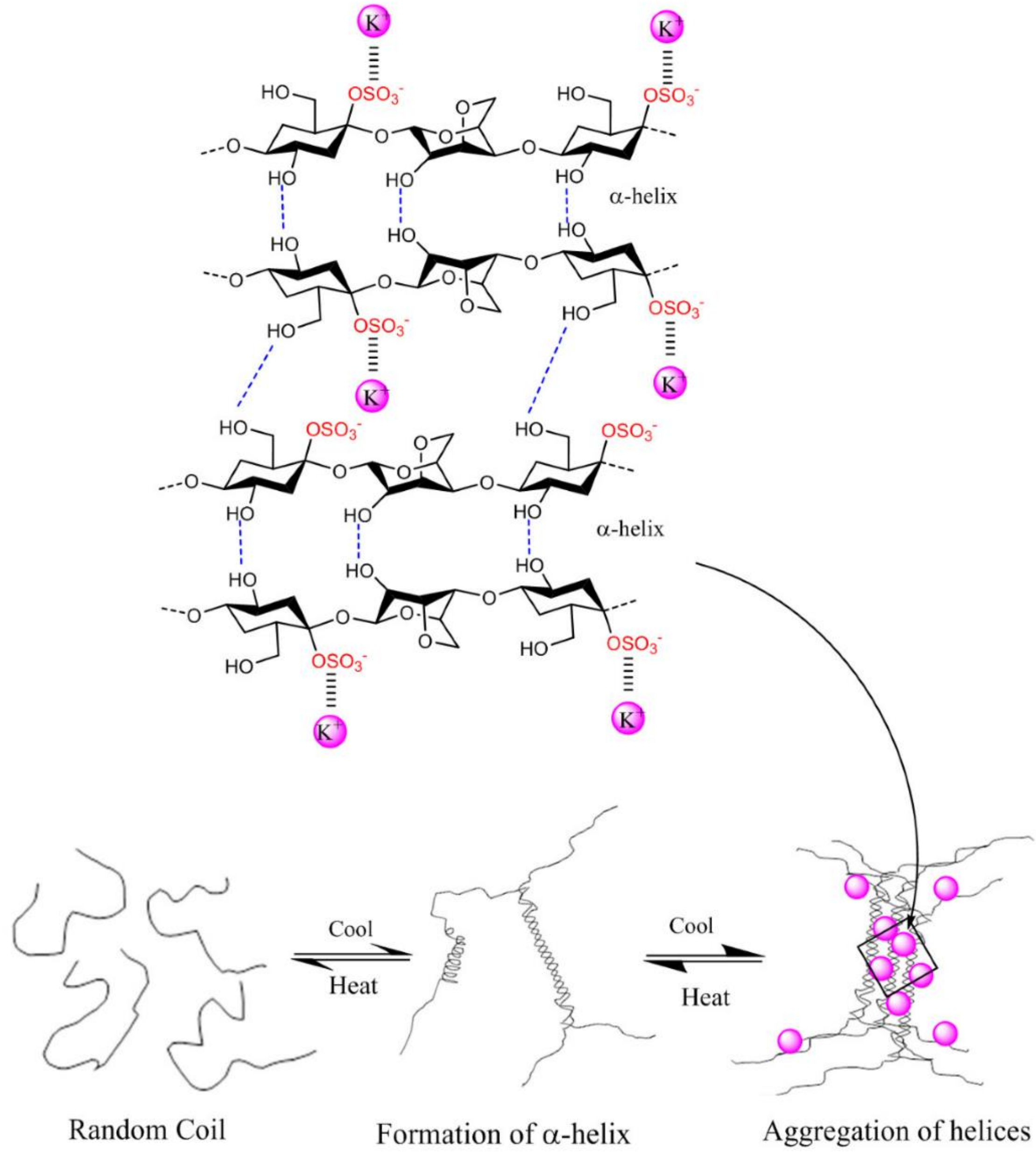


Figure 10 The gelation mechanism of κ-carrageenan in the presence of potassium ions (Reprint from Rhein-Knudsen and coworker, 2015; copyright with permission from MDCI publications) (Rhein-Knudsen *et al.*, 2015)

Table 3 The applications of chitosan, alginate and carrageenan as supporting materials

Supporting materials	Applications	Pore sizes (μm)	Pattern	Analytes	References
Chitosan cryogel	Antifungal dressing	21-51	Monolith	Fungi	Dong *et al.*, 2021
	Trapping	29-54	Monolith	Essential oil	Dinu *et al.*, 2021
	Vortex assisted SPE sorbent	-	Monolith	Herbicides	Jiang *et al.*, 2021
	μ-SPE sorbent	-	Monolith	Tetracycline	Xu *et al.*, 2016
Alginate hydrogel	Adsorbent	0.055	Bead	Endocrine disrupting compounds	Tasmia *et al.*, 2020
	Bio-sorbent	~0.080	Bead	Methylene blue	Mallakpour *et al.*, 2021
	Drug delivery	0.053-0.15	Bead	Probiotic	Kim *et al.*, 2021
	Encapsulation	-	Bead	Humic acids	Cristina *et al.*, 2020
Carrageenan hydrogel	Adsorbent	0.0080-0.038	Bead	Cationic dye	Khoshkho *et al.*, 2021
	Adsorbent	-	Bead	Methylene blue	Jabli *et al.*, 2020
	Enzyme encapsulation	-	Bead	β-galactosidase	Zhang *et al.*, 2016
	Magnetic porous ($CaCO_3$) adsorbent	0.040-0.070	Bead	-	Pishnamazi *et al.*, 2020

3.2 Adsorption materials

Adsorption materials are referred to the components of adsorbent that have the specific properties or structure to interact with target analytes. The main interactions between adsorption materials and analytes are mostly depended on their structure, functional groups and polarity. Appropriate material of the adsorbents should have one or more interactions with analytes such as π-π interaction, electrostatic interaction, hydrophobic interaction or hydrogen bonding. In this thesis, graphene oxide, octadecyl, metal organic frameworks and polymer-based materials were used as adsorption materials for the fabrication of composite adsorbents.

3.2.1 Graphene oxide

Graphene oxide (GOx) is carbon-based material which consists of major single-layer atom of sp^2 hybridized carbon and minor atom of C-OH, epoxy, carbonyl (-C=O) and hydroxyl (-OH) groups **(Figure 11)** (Nasiri *et al.*, 2021). The honeycomb-like network of graphene oxide showed the important ability of good electricity, high thermal stability, large specific surface areas, abundance electrons and hole mobility. Therefore, it widely utilized and applied in various applications such as sensor (Jung *et al.*, 2021; Shanbhag *et al.*, 2021), electrochemical (Chen *et al.*, 2021; Zhao *et al.*, 2021), energy storage (García Lebière *et al.*, 2021; Tokgoz *et al.*, 2021) and sample preparation techniques (Guo *et al.*, 2021; Menazea *et al.*, 2020; Mostafavi *et al.*, 2021). According to many functional groups of graphene oxide, it easy to react or functionalize with other chemical. In sample preparation techniques, graphene oxide is utilized to fabricate adsorbent due to it can interact both polar and non-polar compounds via hydrogen bonding of oxygen atoms or -OH group, π-π and hydrophobic interaction of aromatic ring. For example, the adsorbent based on metal-organic framework type HKUST-1 and UV-irradiated graphene oxide (UV-GOx) was developed for CO_2 adsorption (Varghese *et al.*, 2021), the functionalized of graphene oxide and silver nanoparticles was synthesized for phosphates removal in water samples (Vicente-Martínez *et al.*, 2020), the magnetic nanocomposite of amino-functionalized metal-organic framework, graphene oxide and silica-coated cobalt ferrite was fabricated for neonicotinoid insecticides extraction (Ghiasi *et al.*, 2020), the magnesium-aluminum layered double hydroxide coated on graphene oxide nanosheets was applied for parabens extraction in human breast milk (Manouchehri *et al.*, 2020) and the hydroxypropyl-β-cyclodextrin-polyurethane magnetic nanoconjugates/reduced graphene oxide was developed for removal of chromium and lead ions (Nasiri *et al.*, 2021).

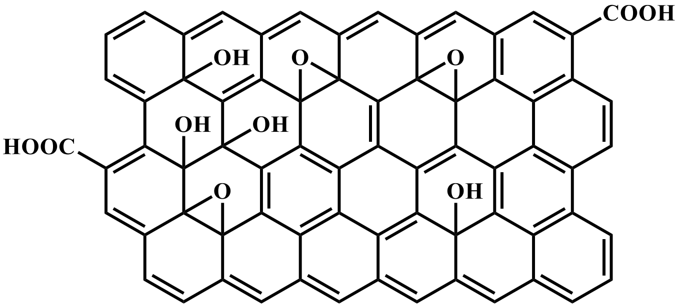


Figure 11 The structure of graphene oxide (GOx)

3.2.2 Octadecyl

Octadecyl (C18) is long hydrocarbon chain which widely utilized as non-polar adsorption material in solid phase extraction techniques due to it provided hydrophobic property. To improve the stability and applicability, octadecylsilane or octadecyl grafted silica (C18@SiO_2) **(Figure 12)** are attend much attention because it simple to modify with different properties of other adsorption materials. The modified C18@SiO_2 with hydrophilic material can cause strong interactions between target analytes and the adsorbent via both hydrophobic and hydrophilic of modified part (Bernardes *et al.*, 2017). For example, the magnetic nanoparticles composited octadecyl modified silica and carbon nanotubes for the extraction of pesticides (Moreno *et al.*, 2018). In addition, octadecyl bonded silica is also quite interesting to apply in magnetic solid phase extraction technique such as C18 functionalized magnetic nanoparticles for phthalic acid extraction (Guo *et al.*, 2014) and octadecyl coated silica magnetite nanoparticles for tetracyclines extraction (Kaewsuwan *et al.*, 2017).

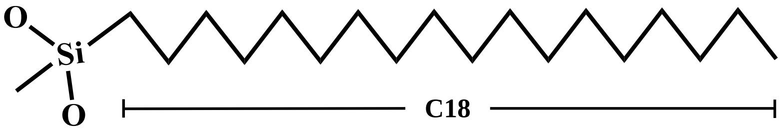


Figure 12 The structure of octadecyl bonded silica (C18@SiO_2)

3.2.3 Metal organic frameworks

Metal organic frameworks (MOFs) are hybrid organic-inorganic porous crystalline structure carbonaceous nanomaterials which produced from coordination bond between building blocks of metal groups and organic linker molecules **(Figure 13)** (Pioquinto-García *et al.*, 2021). The unique properties of MOFs are simple to control pore sizes, consist of large active adsorption sites and high thermal stability (Ibrahim *et al*., 2021; Tchinsa *et al*., 2021). MIL-101(Cr) is an interesting type of MOFs because it provides large specific surface area, spacious macropore sizes and good stable in harsh aqueous solutions (Ghiasi *et al*., 2020). According to the advantages of MIL-101(Cr), it has numerous modified in various sample preparation techniques such as ultrasonic-assisted magnetic solid phase extraction (UA-MSPE) (Ghiasi *et al*., 2020), dispersive solid-phase microextraction (d-SPME) (Zhou *et al.*, 2021) and microwave-assisted magnetic solid-phase extraction (Wang *et al*., 2021).

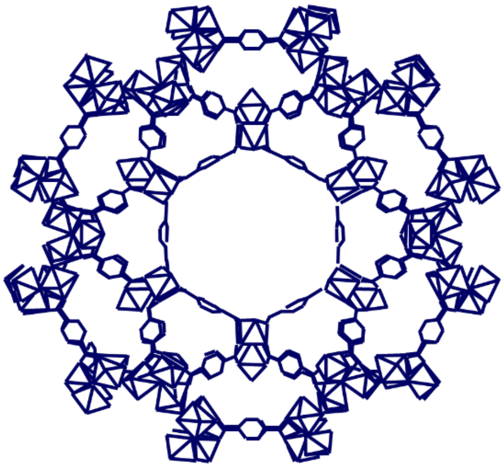


Figure 13 The structure of metal organic frameworks (MOFs)

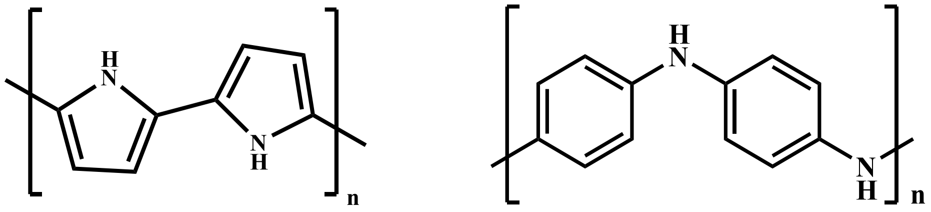
3.2.4 Polymer

Polymers are interesting materials for the fabrication of adsorbents because the potent features of tunable morphologies, multipurpose functional groups, acceptable reusability and simple to synthesize (Moradi *et al.*, 2021; Samadi *et al.*, 2021). The polymeric materials such as polypyrrole (Abdeldaym *et al.*, 2021; Chigondo *et al.*, 2021; Sahu *et al.*, 2021; Stejskal *et al.*, 2021), polyaniline (Abu Taleb *et al.*, 2020; Arora *et al.*, 2021; Maqbool *et al.*, 2020; Park *et al.*, 2021; Tanzifi *et al.*, 2017) and polydopamine (Chen *et al*., 2020; Mu *et al*., 2019; Qi *et al*., 2021; Tong *et al*., 2020; Zhou *et al*., 2019) have been attended increasing attention for the extraction of various target organic compounds in complex matrices of real samples.

Polypyrrole (PPY) is popular polymeric material which widely used to prepare adsorbents for magnetic solid phase extraction (Li *et al.*, 2020; Marsin *et al.*, 2020; Mollahosseini *et al.*, 2019), solid phase extraction (Devasurendra *et al.*, 2018; Seidi *et al.*, 2019; Xie *et al.*, 2019) and solid phase microextraction (Du *et al.*, 2020; Du *et al.*, 2021; Liu *et al.*, 2012; Mametov *et al.*, 2021) techniques due to its unique properties of rapid for polymerization, easy to prepare, good stability, cost effectiveness and good electrical conductivity (do Nascimento *et al*., 2019; Karthikeyan *et al*., 2021). PPY contains aromatic ring and amino group **(Figure 14A)** which suitable for the adsorption of organic compounds via π-π, hydrophobic interaction, hydrogen bonding and electrostatic interaction (Kang *et al.*, 2021).

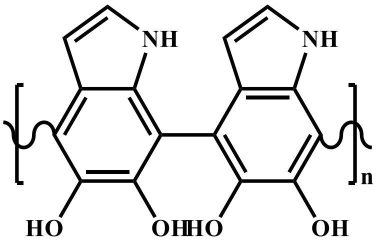
Polyaniline (PANI) is conducting polymer which extensively applied in different field of applications such as electrochemical (Benny *et al.*, 2021; Sun *et al.*, 2021; Yilmaz Erdogan *et al.*, 2020), energy (Emi Princess Prasanna et al., 2020; Shanmugasundaram *et al.*, 2021), environmental (Al-Zahrani *et al.*, 2021) and adsorption of toxic components (Imgharn *et al.*, 2021; Zhang *et al.*, 2021). For adsorption application, the benzene and amino functional groups of polyaniline **(Figure 14B)** can adsorb various organic compounds via hydrogen bonding of -NH groups, π-π and hydrophobic interaction of benzene rings (Chinnathambi *et al*., 2021; Wang *et al.*, 2021). For example, the magnetic graphene oxide nanocomposite modified polyaniline was developed and used for the extraction of polycyclic aromatic hydrocarbons (PAHs) (Manousi *et al*., 2021), the magnetic-polydopamine core shell nanoparticles coated with polyaniline was synthesized for dye adsorption (Miri *et al.*, 2021) and copper oxide composite polyaniline for adsorption of insecticides (Alizadeh *et al.*, 2021).

Polydopamine (PDA) is also an interesting biopolymer for adsorption materials in sample preparation techniques because it is simple to prepare, has multi-interaction from quinone structure, hydrophilic hydroxyl and amine groups **(Figure 14C)** which provide high adsorption capacity and low toxicity (Gonzales *et al.*, 2021; He *et al.*, 2021). The special property of polymerization process of polydopamine is selfpolymerization reaction of dopamine monomers in alkaline or buffer solution under mild conditions (Tian *et al.*, 2021; Zhao *et al.*, 2021; Felfel *et al.*, 2021). According to the advantages of polydopamine, it was developed and applied in sample preparation method such as core-shell composite magnetic-polydopamine nanoparticles for the extraction of copper in foods (Yavuz *et al.*, 2018), magnetic modified polydopamine as dispersive solid phase extraction of sulfonylurea herbicides (Wang *et al.*, 2019) and composite ZIF-7 and polydopamine coated magnetic nanoparticles for PAHs extraction (Zhang *et al.*, 2016).



Polypyrrole (A)

Polyaniline (B)



Polydopamine (C)

Figure 14 The chemical structure of polypyrrole (A), polyaniline (B) and polydopamine (C)

Various adsorption materials were utilized for the fabrication of adsorbents depended on their structure, properties and interactions with analytes as demonstrated in **Table 4**. According to the structure of carbamate pesticides, fluoroquinolones and parabens, the possible interaction including π-π, electrostatic, hydrophobic interaction and hydrogen bonding. Therefore, graphene oxide, octadecyl, MIL-101(Cr) and polymer (polypyrrole, polyaniline and polydopamine) were used for the fabrication of composite adsorbents in this thesis.

Table 4 Sample preparation techniques for the extraction of organic compounds

Sample preparation techniques	Adsorbents	Analytes	Interactions	Recovery (%)	References
SPE	Crumpled graphene	Chlorophenol	Hydrophobic and π-π interaction	92.0-118	Chu *et al*, 2021
MSPE	ZnMIL-101@MGOx	Cefixime	Electrostatic, π-π interaction and hydrogen bonding	95.7-104	Eskandari *et al*, 2021
DμSPE	PVA@MGOx	Organophosphorus pesticides	Electrostatic, π-π interaction and hydrogen bonding	94.5-107	Nasiri *et al*, 2021
MSPE	$CoFe_2O_4$@SiO_2-C18	Triclosan	Hydrophobic, π-π interaction and anion exchange	-	Caon *et al*, 2020
LPME	C18-modified borosilicate disk	Triazine herbicides	Hydrophobic	70.0-130	Roldán-Pijuán *et al*, 2013
SPE	poly(C18 $VIm^+NapSO_3^-$) @SiO_2	Flavonoids	Hydrophobic, π-π interaction, electrostatic and hydrogen bonding	83.6-114	Wang *et al*, 2019

Table 4 Sample preparation techniques for the extraction of organic compounds (continued)

Sample preparation techniques	Adsorbents	Analytes	Interactions	Recovery (%)	References
DMSPE-DLLME-SFO	MIL-101(Cr)	Pantoprazole	Electrostatic, π-π interaction	73.2-78.5	Cai *et al*, 2019
d-SPE	MIL-101(Cr), MIL-100(Fe) and MIL-53(Al) (7:1:2)	Oxytetracycline, tetracycline, chlortetracycline and doxycycline	Electrostatic, π-π interaction	88.1-126	Pang *et al*, 2021
HF-SPE	MIL-101(Cr)@GOx	Diazinon and chlorpyrifos	Electrostatic, π-π interaction and hydrogen bonding	91.0-103	Darvishnejad *et al*, 2020
Packed-fiber SPE	PPY electrospun nanofibers	Folic acid, cyanocobalamin and riboflavin	Electrostatic, π-π interaction and hydrogen bonding	84.9-125	Xie *et al*, 2019
spin-column mSPE	PA-gGOx-PPY electrospun nanofibers	Parabens	Hydrophobic, π-π interaction and hydrogen bonding	81.7-97.8	Seidi *et al*, 2019

Table 4 Sample preparation techniques for the extraction of organic compounds (continued)

Sample preparation techniques	Adsorbents	Analytes	Interactions	Recovery (%)	References
MSPE	Fe_3O_4@PPY	Folic acid and riboflavin	Electrostatic, π-π interaction and hydrogen bonding	92.2-105	Kang *et al*, 2021
D-µSP	CuO nanoplate-polyaniline	Diazinon and Imidacloprid	Electrostatic, π-π interaction and hydrogen bonding	87.0-99.0	Alizadeh *et al*, 2021
MSPE	Fe_3O_4@GOx-PANI	Nitrated polycyclic aromatic hydrocarbons	Hydrophobic, π-π interaction and electrostatic	91.6-114	Manousi *et al*, 2021
SPE	MWCNTs/ZIF-67/PANI	Polycyclic aromatic hydrocarbons	Hydrophobic, π-π interaction and electrostatic	83.4-111	Hajializadeh *et al*, 2020
PT-µSPE	Melamine foam@PANI	Psychotropic drug	π-π interaction, hydrogen bonding and dipole-dipole	80.0-109	He *et al*, 2021
SBSE	$CoFe_2O_4$@PDA	Nitro musks	Hydrophobic and π-π interaction	91.0-120	Grau *et al*, 2021

4. Optimization of the extraction condition

The extraction efficiency of the developed methods depended on various parameters such as amount of adsorbent, sample volume, sample pH and ionic strength, sample flow rate or stirring rate, extraction time and desorption conditions. To achieve the highest extraction efficiency, these parameters were optimized and evaluated in terms of recovery.

4.1 Amount of adsorbent

The amount of adsorbent is basically affected to the extraction recovery. To obtain the highest extraction efficiency, different amount of adsorbents were optimized. The lowest dose of adsorbents that provided the highest recovery were selected as optimal condition for each sub-project.

The optimal adsorbent dosage of PANI/C18@SiO_2@Fe_3O_4/GOx/Algi and PDA/MIL-101/Fe_3O_4/Carr bead were 0.50 g **(Paper II)** and 0.75 g **(Paper III)**, respectively. In case of PPY/C18/GOx/Chi SPE sorbent **(Paper I)**, the amount of sorbent was fixed at 0.50 g **(Table 5)**.

Table 5 Effect of amount of adsorbent on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Amount of adsorbent range (g)	Optimum amount of adsorbent (g)	Recovery (%)	RSD (%)	References
PPY/C18/GOx/Chi	Carbamate pesticides	-	0.50	88.1-93.6	<4.0	**Paper I**
PANI/C18@SiO_2@Fe_3O_4/GOx/Algi	Fluoroquinolones	0.25-1.0	0.50	82.4-88.3	<5.0	**Paper II**
PDA/ MIL-101/Fe_3O_4/Carr	Parabens	0.25-1.0	0.75	84.2-94.3	<4.0	**Paper III**

4.2 Sample volume

The pre-concentration factor of the developed methods is directly depended on the volume of sample solution. However, it also has limitation of adsorption capacity of the adsorbents. Thus, sample volume is an important to be optimized. The highest volume of sample solution which provide the highest extraction efficiency was chosen in extraction procedure. The sample volume were 20.0 mL for **Paper I**, 10.0 mL **for paper II** and **III (Table 6)**. The developed porous composite adsorbents can be used to pre-concentration of target analytes in real samples.

Table 6 Effect of sample volume on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Range of sample volume (mL)	Optimum sample volume (mL)	Recovery (%)	RSD (%)	References
PPY/C18/ GOx/Chi	Carbamate pesticides	5.00-50.0	20.0	88.7-101	<6.0	**Paper I**
PANI/C18@ SiO_2@Fe_3O_4 /GOx/Algi	Fluoroquinolones	5.00-20.0	10.0	86.4-92.3	<5.0	**Paper II**
PDA/ MIL-101/Fe_3O_4/ Carr	Parabens	5.00-20.0	10.0	90.6-96.7	<4.0	**Paper III**

4.3 Sample pH

Sample pH significantly affect the stability and the extraction ability of the adsorbents due to the form of analyte can change under varying the sample pH which influence the interaction of the adsorbents and target analytes. For example, the interaction between PANI/C18@SiO_2@Fe_3O_4/GOx/Algi adsorbent and fluoroquinolones was destroyed after the pH changed from 7.0 to 11 **(Paper II)**. It might because fluoroquinolones were ionized at pH lower than 7.0 while the alkaline condition dissociated the form of carboxylic group. However, in case of **Paper I** and **III**, the extraction efficiency not significantly decreased because the sample pH did not much affect the interaction of target analytes and adsorbents. Thus, these case no need to adjust the pH before extract the target analytes **(Table 7)**.

Table 7 Effect of sample pH on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Range of sample pH	Optimum pH	Recovery (%)	RSD (%)	References
PPY/C18/ GOx/Chi	Carbamate pesticides	2.0-10	2.0-8.0	88.2-100	<5.0	**Paper I**
PANI/C18@ SiO_2@Fe_3O_4/ GOx/Algi	Fluoroquinolones	3.0-11	7.0	91.6-98.3	<6.0	**Paper II**
PDA/ MIL-101/Fe_3O_4/ Carr	Parabens	4.0-8.0	4.0-8.0	87.2-96.4	<5.0	**Paper III**

4.4 Sample flow rate or stirring rate

Sample flow rate and stirring rate of sample solution affect to the extraction efficiency because the contract rate between analytes and adsorbent depended on the appropriate time. In part of sample flow rate, higher flow rate can reduce the adsorption time but at the same time it also impacts the contact between analytes and adsorbent. Therefore, sample flow rate of sub-project I was studied from 0.50 to 8.0 mL min^{-1}. The great extraction recovery with the highest sample flow rate was 5.0 mL min^{-1} as show in **Table 8 (Paper I)**.

The stirring rate is an important factor in MSPE method because it directly impacted the partition of the analytes and adsorption site of the adsorbents. At low stirring speed, mass transfer of analytes was decreased due to the adsorbents not fully disperse in aqueous solution. On the contrary, the contact of sorbent and analytes was too brief at high speeds. The suitable stirring rate of sample solution by PANI/C18@SiO_2@Fe_3O_4/GOx/Algi **(Paper II)** and PDA/MIL-101/Fe_3O_4/Carr **(Paper III)** adsorbents were 1000 rpm and 800 rpm, respectively **(Table 8)**.

Table 8 Effect of sample flow rate and stirring rate on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Range of sample flow rate or stirring rate	Optimum values	Recovery (%)	RSD (%)	References
PPY/C18/ GOx/Chi	Carbamate pesticides	0.50-8.0 (mL min^{-1})	5.0 (mL min^{-1})	89.1-97.8	<5.0	**Paper I**
PANI/C18 @SiO$_2$@ Fe$_3$O$_4$/GOx /Algi	Fluoroquinolones	500-2000 (rpm)	1000 (rpm)	84.2-93.5	<4.0	**Paper II**
PDA/MIL-101/Fe$_3$O$_4$/ Carr	Parabens	500-1500 (rpm)	800 (rpm)	86.4-90.2	<3.0	**Paper III**

4.5 Extraction time

The adsorption equilibrium is generally affected by the extraction time during the adsorption process. To achieve the highest extraction efficiency with the shortest time, the extraction time of the developed MSPE method were investigated. The highest recovery of the developed MSPE methods for the extraction of fluoroquinolones and parabens were 20.0 min **(Paper II)** and 10.0 min **(Paper III)**, respectively **(Table 9)**.

Table 9 Effect of extraction time on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Range of extraction time (min)	Optimum extraction time (min)	Recovery (%)	RSD (%)	References
PANI/C18 @SiO$_2$@ Fe$_3$O$_4$/GOx /Algi	Fluoroquinolones	10.0-30.0	20.0	88.1-95.5	<6.0	**Paper II**
PDA/MIL-101/Fe$_3$O$_4$/ Carr	Parabens	5.00-30.0	10.0	81.4- 90.2	<5.0	**Paper III**

4.6 Desorption conditions

The appropriate desorption solvent is an important key to desorb analytes from both SPE and MSPE adsorbents. The principles selection of the desorption solvent normally based on like dissolves like role. Thus, various organic solvent with different polarities were considered and investigated. The moderately polar analytes of carbamate pesticides, fluoroquinolones and parabens are suitable with rather polar solvent of acetonitrile **(Paper I)**, the mixture of acetonitrile: dichloromethane: 0.1 M acetic acid (45:45:10) **(Paper II)** and the mixture of acetonitrile: ethyl acetate (1:1) **(Paper III)**, respectively **(Table 10)**. However, the interaction in case of PANI/C18@SiO_2@Fe_3O_4/GOx/Algi and fluoroquinolones **(Paper II)** are quite strong with hydrogen bonding. Therefore, acetic acid was added in desorption solvent to break up the interaction between the adsorbent and fluoroquinolones.

To reduce the hazard from organic solvents, the volume of desorption solvents was optimized with the criteria of the lowest volume of organic solvents that provided the highest extraction recovery. The desorption solvent volume for PPY/C18/GOx chitosan cryogel sorbent **(Paper I)** and PANI/C18@SiO_2@Fe_3O_4/GOx alginate beads **(Paper II)** were 3.0 mL. While, the mixture solvents for the developed method of PDA/MIL-101/Fe_3O_4 carrageenan beads **(Paper III)** was 2.0 mL **(Table 11)**.

Table 10 Effect of type of desorption solvent on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Type of desorption solvent	Optimum desorption solvent	Recovery (%)	RSD (%)	References
PPY/C18/GOx/Chi	Carbamate pesticides	Methanol Acetone Acetonitrile Ethanol Ethyl acetate Propanol	Acetonitrile	92.8-99.1	<6.0	**Paper I**
PANI/C18@SiO_2@Fe_3O_4/GOx/Algi	Fluoroquinolones	Methanol Acetonitrile Dichloromethane Acetonitrile:dichloromethane (1:1) Acetonitrile:dichloromethane: acetic acid 0.1 M (45:45:10)	Acetonitrile:dichloromethane: acetic acid 0.1 M (45:45:10)	84.4-91.7	<6.0	**Paper II**
PDA/MIL-101/Fe_3O_4/Carr	Parabens	Methanol Acetone Acetonitrile Ethyl acetate Acetonitrile:ethyl acetate (1:1)	Acetonitrile:ethyl acetate (1:1)	81.6-86.3	<5.0	**Paper III**

Table 11 Effect of volume of desorption solvent on the extraction recovery of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Volume of desorption solvent (mL)	Optimum volume of solvent (mL)	Recovery (%)	RSD (%)	References
PPY/C18/ GOx/Chi	Carbamate pesticides	1.0-4.0	3.0	90.5-98.7	<7.0	**Paper I**
PANI/C18 @SiO_2@ Fe_3O_4/GOx /Algi	Fluoroquinolones	2.0-5.0	3.0	88.2-95.5	<5.0	**Paper II**
PDA/MIL-101/Fe_3O_4/ Carr	Parabens	1.0-4.0	2.0	90.3-94.6	<5.0	**Paper III**

5. Analytical performance

The analytical performances of the developed methods were evaluated including linear dynamic range (LDR), limit of detection (LOD), limit of quantification (LOQ), accuracy, precision, reproducibility and reusability. These terms were studied under optimum conditions of the each developed SPE and MSPE techniques.

5.1 Linear dynamic range

Linear dynamic range (LDR) is the capability of the analytical methods which demonstrate the concentration of target analytes in real samples. The calibration curve of LDR is plot between the average concentration of analytes spiked in sample (x-axis) and the response value (y-axis). The LDRs are generally operated in 3 replications with 4 or more different concentrations of spiked standard solution. The acceptable linear regressions follow by AOAC are established at the coefficient of determination (R^2) higher than 0.99 (AOAC, 2016). The linearity in this thesis were plotted between peak area and the concentration of carbamate pesticides, fluoroquinolones and parabens in unit of $\mu g\ L^{-1}$. The LDRs of **Paper I-III** showed R^2 higher than 0.99 **(Table 12)**. It indicated that the developed methods have good linear range for the determination of target analytes at trace concentrations.

Table 12 Linear dynamic range and coefficients of determination (R^2) of the developed methods

Adsorbent	Samples	Analytes	Linear range ($\mu g\ L^{-1}$)	R^2	Reference
PPY/C18/GOx/Chi	Fruit juices	Carbamate	0.5- 500	0.9993-1.0000	**Paper I**
PANI/C18@SiO_2@Fe_3O_4/GOx/Algi	Foods	Fluoroquinolones	0.001-50	0.9933-0.9994	**Paper II**
PDA/MIL-101/Fe_3O_4/Carr	Personal care products	Parabens	0.1-100	0.9968-0.9986	**Paper III**

5.2 Limit of detection and limit of quantification

Limit of detection (LOD) is normally specified as the lowest concentration of target analytes which can be trusty detected under optimum conditions of the analytical methods. The limit of quantification (LOQ) is set as the lowest concentration of analytes in sample that can be measured with acceptable precision. There are several strategies to calculate the LODs and LOQs depended on the analytical techniques. According to the recommendation from EURACHEM guideline, in this thesis, the LODs and LOQs were carried out based on signal to noise ratio (S/N) or peak area of noise to peak area of the analytes at 3 folds or higher ($S/N \geq 3$) for LODs and 10 folds or greater ($S/N \geq 10$) for LOQs (Magnusson and Örnemark, 2014).

In this thesis, the LODs and LOQs of the developed solid phase extraction of PPY/C18/GOx/Chi adsorbent **(Paper I)** and magnetic solid phase extraction techniques of PANI/C18@SiO_2@Fe_3O_4/GOx/Algi beads **(Paper II)** and PDA/MIL-101/ Fe_3O_4/Carr beads **(Paper III)** are summarized in **Table 13**. These results indicated that the developed sample preparation methods can be applied for the extraction, enrichment and determination of target analytes at trace levels.

Table 13 The LODs and LOQs of three developed adsorbents based on solid phase extraction and magnetic solid phase extraction techniques

Paper I: The PPY/C18/GOx chitosan cryogel adsorbent for the extraction of carbamate pesticides from standard solution

Carbamate pesticides	LODs (μg L^{-1})	LOQs (μg L^{-1})
Carbofuran	1.0	4.0
Carbaryl	0.50	1.5
Isoprocarb	2.0	8.0
Diethofencarb	1.0	4.0

Paper II: The PANI/C18@SiO_2@Fe_3O_4/GOx alginate bead for the extraction of fluoroquinolones from standard solution

Fluoroquinolones	LODs (μg L^{-1})	LOQs (μg L^{-1})
Ciprofloxacin	0.005	0.02
Danofloxacin	0.001	0.003
Diflxacin	0.01	0.04
Enrofloxacin	0.005	0.02
Norfloxacin	0.005	0.02
Sarafloxacin	0.01	0.04

Paper III: The PDA/MIL-101/Fe_3O_4 carrageenan bead for the extraction of parabens from standard solution

Parabens	LODs (μg L^{-1})	LOQs (μg L^{-1})
Methyl paraben	0.050	0.10
Ethyl paraben	0.15	0.50
Propyl paraben	1.0	2.5
Butyl paraben	1.0	2.5

5.3 Accuracy

The accuracy of sample preparation methods in analytical techniques are generally measured in term of recovery with non-spiked and spiked standard solution into sample under linear concentration levels. To study the efficiency of the developed methods, the sample were spiked with 3 or more concentration of analytes and replicated 3 times for each concentration. The acceptable recovery depended on analytical methods and concentration range of the analytes. The recommendation acceptable level by AOAC is in the rage of 60.0 to 115% for ppb level (AOAC, 2016). The percentage recovery was calculated using the following equation.

$$\text{Recovery (\%)} \quad = \quad \frac{(C_f - C_u)}{C_a} \times 100$$

Where C_f is the target analytes concentration of spiked sample

C_u is the target analytes concentration of non-spiked sample

C_a is the concentration of analytes added into sample

The recoveries were evaluated at 10, 50 and 100 µg L^{-1} for the porous composite monolith chitosan cryogel sorbent **(Paper I)**, 0.1, 0.5, 1 and 10 µg kg^{-1} for doubly porous composite in alginate beads **(Paper II)** and the range of 5, 10 and 50 µg L^{-1} for polydopamine coated porous composite materials embedded in carrageenan beads **(Paper III)**. The results indicated that the satisfactory recoveries were obtained from 80.4 to 99.5% which in the acceptable range.

5.4 Precision

The precision is defined as the closeness value of various replicative measurement under the optimum condition. The precision is normally represented in the term of percentage of relative standard deviation (%RSD). The acceptable precision established by Association of Official Analytical Chemists (AOAC) is < 21% at ppb level (AOAC, 2016). The RSD (%) can be calculated using the following equation;

$$\text{RSD (\%)} \quad = \quad (SD \div \bar{X}) \times 100$$

Where SD is the standard deviation of measurement

$\bar{X}$ is the mean value of n measurement (n = 3)

The developed porous composite monolith chitosan cryogel sorbent **(Paper I)**, the doubly porous composite in alginate beads **(Paper II)** and the polydopamine coated porous composite materials embedded in carrageenan beads **(Paper III)** exhibited RSD (%) less than 9.0% which acceptable by AOAC. Therefore, it can be concluded that the developed methods can be used for the extraction of target analytes with good precision.

5.5 Reproducibility

The reproducibility of developed methods is usually examined by relative standard deviation of different preparation lots of the synthesized adsorbents under the same preparation and extraction condition. The closeness values of individual results are indicated to precision of the extraction process. The reproducibility of this thesis was studied with six different lots at different times of the preparation process but used to extract the analytes at the same condition. The relative standard deviations of the developed adsorbents were lower than 6.0% **(Paper I-III) (Table 14)** which in acceptable range by AOAC guideline (less than 16% for ppb level) (AOAC, 2016). These results confirm that the preparation strategies of all developed adsorbents have good reproducibility.

Table 14 The reproducibility of the developed adsorbents for the extraction of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Lots of adsorbents (Number)	Recovery (%)	RSD (%)	References
PPY/C18/GOx/Chi	Carbamate pesticides	6	86.4-98.2	<6.0	**Paper I**
PANI/C18@ SiO_2@Fe_3O_4/GOx/Algi	Fluoroquinolones	6	82.7-91.6	<5.0	**Paper II**
PDA/MIL-101/Fe_3O_4/Carr	Parabens	6	89.3-93.2	<6.0	**Paper III**

5.6 Reusability

The reusability was investigated to study the physical and chemical stability of the developed adsorbents. The reusability is an important to reduce the time of the extraction process and total cost of the analytical method. The composite adsorbents were clean up with the suitable desorption solvent to remove the memory effect and pre-treatment with deionized water before used in the next extraction cycles. The extraction cycles of PPY/C18/GOx/Chi adsorbent **(Paper I)**, PANI/C18@SiO_2@Fe_3O_4/GOx/Algi beads **(Paper II)** and PDA/MIL-101/Fe_3O_4/Carr beads **(Paper III)** were 13, 7 and 6 times, respectively **(Table 15)**. The stability of the adsorbents is depended on properties of supporting and adsorption materials and type of sample preparation methods.

Table 15 The reusability of the developed adsorbents for the extraction of carbamate pesticides, fluoroquinolones and parabens

Adsorbents	Analytes	Extraction cycles (times)	Recovery (%)	RSD (%)	References
PPY/C18/GOx/Chi	Carbamate pesticides	13	84.4-100	<7.0	**Paper I**
PANI/C18@SiO_2@Fe_3O_4/GOx/Algi	Fluoroquinolones	7.0	82.5-98.6	<4.0	**Paper II**
PDA/MIL-101/Fe_3O_4/Carr	Parabens	6.0	87.3-94.5	<7.0	**Paper III**

6. Conclusion

The solid phase extraction and magnetic solid phase extraction sorbents were successfully synthesized and applied for the extraction and pre-concentration of trace organic compounds in foods and personal care products before analysis with high performance liquid chromatography.

The first project is high porous monolith adsorbent of polypyrrole composite octadecyl silica and graphene oxide embedded in chitosan cryogel (PPY/C18/

GOx/Chi) based solid phase extraction technique for the extraction of carbamate pesticides in fruit juices before analysis with HPLC-DAD **(Paper I)**. This developed SPE adsorbent can solve the main problem of high backpressure using high porosity of chitosan cryogel as supporting material. Another good reason of high porous composite adsorbent is used less extraction time because it can flow sample solution passthrough sorbent at high flow rate. Moreover, the composite adsorption materials of graphene oxide, octadecyl and polypyrrole can help to adsorb carbamate pesticides with strong interaction. It provided good extraction efficiency (extraction recovery >84%), wide linear range responses from 0.5 to 500 µg L^{-1}, low limit of detection in the range of 0.5 to 2 µg L^{-1}, good accuracy, precision and can be reused at least 13 extraction cycles.

The second project is the doubly porous composite of polyaniline, octadecyl-bonded silica magnetite nanoparticles and graphene oxide (PANI/C18@SiO_2@ Fe_3O_4/GOx) incorporated in alginate beads based magnetic solid phase extraction technique for the extraction and enrichment of fluoroquinolones antibiotics in eggs, honey and milk before analysis with HPLC-FLD **(Paper II)**. Magnetite nanoparticles in the composite hydrogel adsorbent was utilized the special key to separate the adsorbent from aqueous sample or organic solvent which simple reaction between external magnet and Fe_3O_4 nanoparticles. The distinctive point of this developed MSPE adsorbent is doubly porous network which created from the reaction between $CaCO_3$ inside alginate beads and hydrochloric acid. The double porosity of the composite adsorbent can increase the surface area of hydrogel bead that help to improve the adsorption site and easy to coat with polyaniline. The composite materials of graphene oxide, polyaniline and octadecyl used to adsorb target analytes via π-π interaction, hydrogen bonding and hydrophobic interaction. Therefore, this double porous composite alginate hydrogel sorbent provided high extraction efficiency with recovery higher than 80%, low limit of detection (0.001 - 0.01 µg L^{-1}), good precision and chemical stability which can be reused up to 7 times.

The last project is polydopamine coated composite materials between metal organic framework and Fe_3O_4 nanoparticles embedded in porous carrageenan beads (PDA/MIL-101/Fe_3O_4/Carr) for the extraction and pre-concentration of parabens in personal care products before analysis with HPLC-DAD **(Paper III)**. This developed composite adsorbent based on magnetic solid phase extraction is provides the both advantages of double porous hydrogel and magnetic properties. Carrageenan supporting material are exhibited good biodegradability after colossally used, low toxicity and environmentally friendly. In addition, polydopamine and metal organic framework type MIL-101(Cr) are good adsorption materials to interact with parabens. This composite PDA/MIL-101/Fe_3O_4 incorporated in carrageenan beads also exhibited good extraction efficiency for parabens (recovery 80-96%), low limit of detection, good reproducibility and reusability.

In summary, the developed SPE and MSPE adsorbents were successfully fabricated and applied for the extraction and pre-concentration of carbamate pesticides, fluoroquinolones and parabens in foods samples (fruit juices, eggs, honey and milk) and personal care products. The developed methods have good extraction efficiency, low limit of detection and good accuracy and precision. The advantages of these high porous composite adsorbents are simple to fabricate, easy to use, can reduce the extraction time and environmentally friendly. In addition, these developed porous composite adsorbent may adapt to extract other organic materials in various kind of samples.

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Appendices

Paper I

Klongklaew, P., Naksena, T., Kanatharana, P., Bunkoed, O., A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices. ***Analytical and Bioanalytical Chemistry*** 410(27) (2018), 7185-7193.

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RESEARCH PAPER

A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices

Pattamaporn Klongklaew[1,2] · Thamolwan Naksena[1,2] · Proespichaya Kanatharana[1,2] · Opas Bunkoed[1,2]

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Abstract

A hierarchically porous structured composite monolith sorbent of polypyrrole-coated graphene oxide and octadecyl silica incorporated in chitosan cryogel (PPY/GOx/C18/chitosan) was synthesized and used as solid-phase extraction sorbent for the determination of carbamate pesticides. Various factors affecting the characteristics of the adsorbents (chemistry of the sorbent, polymerization time, concentrations of graphene oxide and octadecyl silica) and the extraction efficiency using the prepared sorbents, such as sample loading, desorption conditions, sample volume, sample flow rate, sample pH, and ionic strength, were investigated and optimized. Under the optimal conditions of sorbent preparation and extraction, the developed composite monolith sorbent provided wide linear responses from 1.0 to 500 μg L^{-1} for carbofuran and diethofencarb, from 0.5 to 500 μg L^{-1} for carbaryl, and from 2.0 to 500 μg L^{-1} for isoprocarb. The limits of detection using HPLC-UV at 203, 220, and 208 nm were in the range of 0.5–2.0 μg L^{-1}. When the composite monolith sorbent was applied for the pre-concentration and determination of carbamate in fruit juices, good recoveries (84.1–99.5%) were achieved. The developed sorbents were porous and exhibited low back pressure enabling their use at high flow rates during sample loading. Extraction and clean-up were highly efficient, and the good physical and chemical stability of the sorbent enables reuse up to 13 times.

Keywords Carbamate · Polypyrrole · Octadecyl silica · Graphene oxide · Chitosan cryogel · Monolith

Introduction

Carbamate pesticides are extensively used to control insects and fungi in agriculture [1, 2]. Their popularity is due to their high efficacy and low cost. However, excessive use of these pesticides may leave residues in environmental and agricultural products such as wine and fruit juices [3, 4]. Their residues in food could have adverse effects on human health such as vomiting, headache, and uncontrolled urination [5, 6]. The European Union has established a maximum permissible concentration for total pesticides of 0.5 μg L^{-1} in drinking water. Therefore, the monitoring of carbamate pesticide residues in agricultural products is an important aspect of food safety. The analytical techniques that have been used for the analysis of carbamate pesticides include high-performance liquid chromatography (HPLC) [7–9], electrochemical detection [10], biosensors [11, 12], and capillary electrophoresis (CE) [13, 14]. However, because residues of carbamate pesticides in agricultural products are normally present at low concentrations and contain various matrix interferences, a sample preparation procedure is necessary to pre-concentrate and clean-up the samples before analysis to improve the detectability of the analytes of interest. Several sample preparation methods are used for the pre-concentration and pre-treatment of carbamate pesticides. The techniques used include liquid–liquid extraction (LLE) [15], solid-phase extraction (SPE) [16], solid-phase microextraction (SPME) [17], stir bar sorptive extraction

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✉ Opas Bunkoed
opas.b@psu.ac.th

[1] Trace Analysis and Biosensor Research Center, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

[2] Center of Excellence for Innovation in Chemistry, Department of Chemistry, Faculty of Science, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

(SBSE) [1, 18], and dispersive liquid–liquid microextraction (DLLME) [19, 20]. However, all these techniques have drawbacks. LLE generally uses large volumes of toxic solvents and is time-consuming. SPME and SBSE are time-consuming and the fragility and expense of the fibers and stir bars needed for these techniques are also disadvantages. The limitation of DLLME is the importance of selecting the appropriate extraction solvent [20]. For trace analysis in complex samples, SPE has attracted much attention due to its convenience, easy operation, high enrichment factors, and good extraction efficiency. To increase the sample flow rate and reduce back pressure of SPE sorbent, an interesting avenue is the development of an easily synthesized porous structured monolith SPE sorbent. A good platform for this type of sorbent is chitosan cryogel because it has a sponge-like structure which can be used to entrap nanomaterials in the macropores or on its surfaces [21, 22]. In addition, it is non-toxic, low cost, and biodegradable [23]. Integrating materials with different properties in the porous monolith sorbent is an interesting approach to increase the extraction efficiency of the sorbent while maintaining a fast extraction procedure. In this regard, graphene oxide, octadecyl silica, and polypyrrole are interesting adsorption materials due to their good chemical stability and large surface area [24–26]. The structure of graphene oxide presents hydroxyl, epoxide, and carboxylic functional groups [27, 28], which can adsorb carbamate through hydrogen bonding and π-πinteraction. Polypyrrole can also adsorb carbamate via hydrogen bonding and π-πinteraction, while octadecyl silica can adsorb carbamate via hydrophobic interaction.

This work presents a composite monolith sorbent of graphene oxide and octadecyl silica, embedded in porous chitosan cryogel and coated with polypyrrole. The sorbent was prepared and used for the pre-concentration of carbamate pesticides for subsequent analysis by HPLC-UV in reversed phase mode. The important parameters affecting the extraction efficiency including the type of adsorbent, polymerization time, amount of graphene oxide and C18, desorption conditions, sample volume, sample pH, sample flow rate, and ionic strength were studied and optimized. Finally, the analytical performance of the developed sorbent was validated.

Materials and methods

Chemicals and materials

Chitosan from shrimp shells, graphene oxide powder (4–10% edge-oxidized, 15–20 sheets, octadecyl silica (C18), pyrrole, glutaraldehyde, iron (III) chloride hexahydrate, carbofuran, carbaryl, isoprocarb, and diethofencarb were from Aldrich (Steinheim, Germany). Acetonitrile, methanol, acetic acid, and 2-propanol were from Labscan (Bangkok, Thailand). Deionized water was obtained from a Maxima water ultra-purification system (Elgastat Maxima, ELGA, UK).

Instrumentals

HPLC analysis was carried out on an Agilent 1100 HPLC system equipped with a diode array detector (Agilent Technologies, Germany). The separation of carbamate pesticides was performed on a VertiSep™ UPS C18 column (4.6 mm × 150 mm i.d., 5-μm particle size, Restek, USA) at 30 °C. The mobile phase consisted of methanol and water (63:37% *v*/*v*) and its flow rate was 0.90 mL min^{-1}. The detection wavelength was set at 203 nm for carbofuran, 220 nm for carbaryl, and 208 nm for isoprocarb and diethofencarb. The FTIR spectra were recorded with an FTIR spectrometer from PerkinElmer (MA, USA). The morphology of the as-prepared sorbent was examined by JSM 5200 scanning electron microscopy (SEM) (JOEL, Japan). The specific BET surface areas were determined using a Quantachrome Autosorb 1 system (Quantachrome Instruments, USA).

Preparation of composite monolith polypyrrole/graphene oxide/C18/chitosan cryogel sorbent

Two grams of chitosan powder was completely dissolved in 100 mL of 0.10 M acetic acid. Then, 0.10 g of graphene oxide was added to this chitosan solution (1.0% *w*/*v*) and stirred at 1500 rpm for 30 min to obtain a homogeneous solution. Next, 1.0 g of octadecyl silica was added and stirred at 1000 rpm for 1 h. Subsequently, 1.0 mL of the mixture solution was poured into an empty 5.0-mL polypropylene cartridge and 30 μL of glutaraldehyde was added to the solution. The cartridge was vortexed for 10 s and then placed in a freezer at − 20 °C. After freezing for 12 h, the composite monolith GOx/C18/chitosan cryogel was obtained by thawing the cartridge at room temperature (27 ± 1 °C). To further modify the composite GOx/C18/chitosan cryogel, 2.0 mL of 2-propanol was added to the cartridge, followed by 400 μL of pyrrole monomer and 2.0 mL of ferric chloride solution. The oxidation polymerization progressed at room temperature (27 ± 1 °C) for 1 h. At this point, the synthesis of the composite monolith PPY/GOx/C18/chitosan cryogel sorbent was completed and the prepared sorbent was washed with 5.0 mL of 2-propanol, then with methanol and lastly with deionized water. Figure 1 illustrates the preparation of composite monolith PPY/GOx/C18/chitosan cryogel sorbent. The different types of monolith sorbents were also prepared and its chemical composition as shown in the Electronic Supplementary Material (ESM) Table S1.

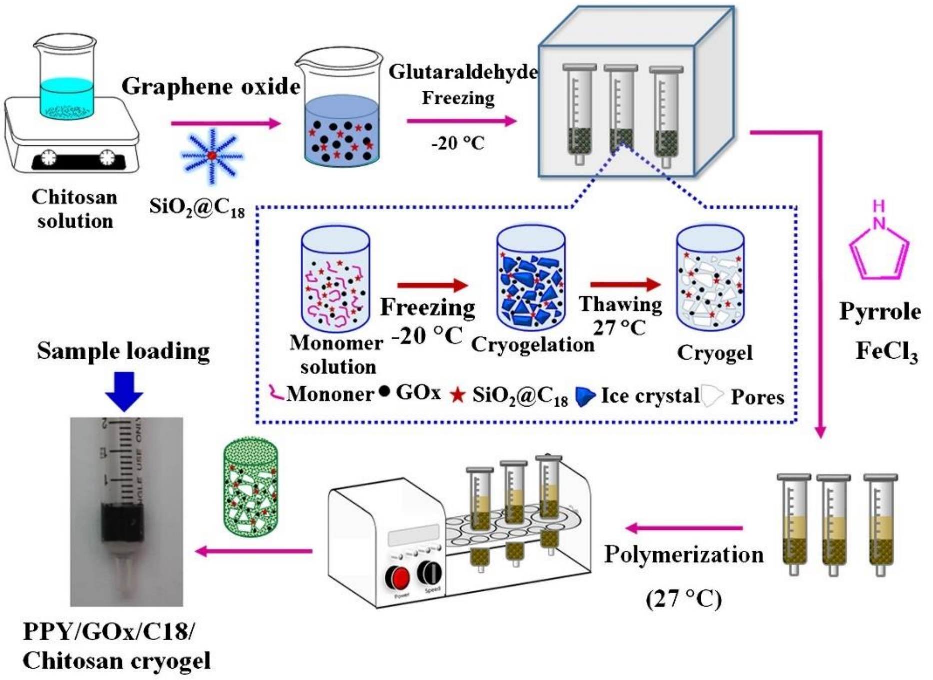

Fig. 1 Schematic diagram of the preparation of the composite monolith PPY/GOx/C18/chitosan cryogel sorbent

Solid-phase extraction procedure

The composite monolith PPY/GOx/C18/chitosan cryogel sorbent was formed within the confines of an empty SPE polypropylene cartridge. Solid-phase extraction was performed using a vacuum manifold. Before loading the sample, the developed sorbent was activated with 1.0 mL of acetonitrile followed by deionized water (1.0 mL). Then, 20.0 mL of sample solution was loaded through the sorbent at a constant flow rate of 5.0 mL min^{-1}. Afterwards, the retained analytes were eluted with 3.0 mL of acetonitrile. The eluent was then evaporated to dryness at 55 °C and re-dissolved in 0.50 mL of methanol-water (63:37% *v*/*v*). Finally, 20 μL of the resulting solution was injected into the HPLC system.

Real samples

All samples were purchased from local markets in Songkhla province, Thailand. Before loading through the developed sorbent, the fruit juice samples were filtered through a 0.45-μm filter to remove solid particles that could block the pores of the sorbent and obstruct adsorption of the analytes.

Results and discussion

Characterization of composite monolith polypyrrole/graphene oxide/C18/chitosan cryogel sorbent

FTIR analysis confirmed the functional groups of the as-prepared composite monolith sorbent. As shown in ESM Fig. S1, the spectrum of chitosan (a) shows the characteristic absorption band at 3430 cm^{-1} attributed to –OH. The peaks at 1720 and 1590 cm^{-1} are attributed to C=O stretching and N–H bending vibration, respectively. The peak at 2930 cm^{-1} is due to symmetric –CH$_2$ stretching vibration [29]. The bands at 1320 and 1070 cm^{-1} correspond to the stretching of C–O–N and C–O groups. The FTIR spectrum of SiO$_2$–C18 (b) shows a strong absorption region at 1100 to 1200 cm^{-1} which corresponds to the Si–O–H and Si–O–Si bonds. The absorption peaks at 2852 and 2920 cm^{-1} are related to the C–H stretching vibration of the octadecyl group [30]. The FTIR spectrum of graphene oxide (c) shows characteristic peaks at 690 cm^{-1} corresponding to C–H, peaks at 1505 cm^{-1} due to C–H bending vibration, at 1732 cm^{-1} due to C=O stretching vibration, and at 3430 cm^{-1} due to the O–H stretching vibration [31]. The FTIR spectrum of polypyrrole (d) shows absorption peaks at 1200 and 1540 cm^{-1} attributed to the absorption peaks of the pyrrole ring. The peak at 950 cm^{-1} was attributed to C–H wagging. The FTIR spectrum of the as-prepared composite monolith PPY/GOx/C18/chitosan cryogel sorbent (e) indicated that graphene oxide, SiO_2–C18 and polypyrrole were successfully composited within the chitosan cryogel.

The morphology of the chitosan cryogel, C18/chitosan cryogel, and composite monolith PPY/GOx/C18/chitosan cryogel sorbent was observed by SEM. As can be seen in Fig. 2a, b, the surface of the chitosan cryogel was smooth. The SEM images of composite C18/chitosan cryogel (Fig. 2c, d) indicated that the C18 silica was entrapped in the chitosan cryogel. The surface of the composite monolith PPY/GOx/C18/chitosan cryogel had a rough surface of uniformly distributed grains (Fig. 2e, f). In addition, the typical interconnected skeletal structure of monolith cryogels can be clearly observed. The high porosity of composite cryogels helps to reduce the back pressure that normally occurs in conventional particles packed SPE cartridges.

The surface areas of the chitosan cryogel, C18/chitosan cryogel, GOx/chitosan cryogel, PPY/chitosan cryogel, GOx/C18/chitosan, PPY/C18/chitosan, PPY/GOX/chitosan, and the composite monolith PPY/GOx/C18/chitosan cryogel sorbent were calculated using BET theory as shown in ESM Table S2. The surface area of the composite monolith PPY/GOx/C18/chitosan sorbent, being significantly larger than the surface area of the chitosan cryogel, has more abundant adsorption sites which should improve adsorption of the target analytes. Thus, it can be expected that the modification of the developed composite monolith cryogel sorbent will improve extraction efficiency. In addition, the composite monolith PPY/GOx/C18/chitosan cryogel sorbent allows fast diffusion of the target analyte, achieving extraction equilibrium rapidly.

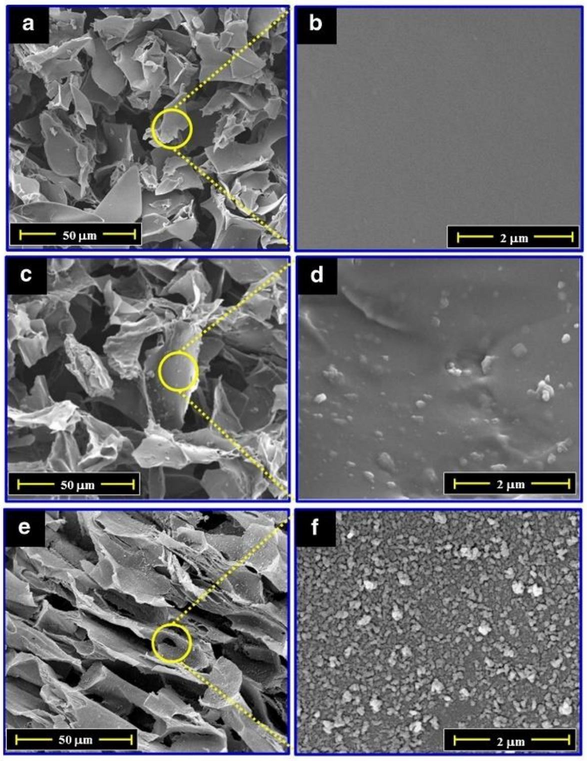

Fig. 2 SEM images of chitosan cryogel × 1000 (**a**) and × 20,000 (**b**), C18/chitosan cryogel × 1000 (**c**) and × 20,000 (**d**), and composite monolith PPY/GOx/C18/chitosan cryogel sorbent × 1000 (**e**) and × 20,000 (**f**)

Optimization of solid-phase extraction

To obtain the highest extraction efficiency in the shortest analysis time with the lowest solvent consumption, various important parameters affecting extraction efficiency were optimized. These parameters were as follows: the type of sorbent, polymerization time, concentrations of graphene oxide and octadecyl silica deposited, desorption conditions, sample volume, sample flow rate, sample pH, and ionic strength.

Comparison of different types of sorbent

The extraction efficiency of different types of monolith sorbents was investigated (Fig. 3). The extraction recoveries of carbamate pesticides using chitosan cryogel, C18/chitosan, GOx/chitosan, PPY/chitosan, GOx/C18/chitosan, PPY/C18/chitosan, PPY/GOx/chitosan, and PPY/GOx/C18/chitosan are summarized in ESM Table S2. The composite monolith PPY/GOx/C18/chitosan cryogel sorbent provided the highest extraction efficiency because it had more adsorption sites and higher surface areas than the other sorbents. Three interactions can occur between the composite monolith PPY/GOx/C18/chitosan cryogel sorbent and carbamate pesticide molecules. These are hydrogen bonding, hydrophobic, and π-πinteractions (ESM Fig. S2).

Effect of polymerization time

The polypyrrole component of the sorbent was prepared by oxidation polymerization (ESM Scheme S1) at room temperature (37 ± 1 °C). The effect of the polymerization time of the polypyrrole was investigated by varying the polymerization time from 0.5 to 6.0 h and comparing the extraction of carbamate pesticides by the prepared sorbents. The recoveries of the extractions are shown in Fig. 4a. The recovery increased with increased polymerization time from 0.5 to 1.0 h but slightly decreased with further increments of polymerization time. The longer polymerization times produced polypyrrole layers that were too thick. The thickness of the polypyrrole layers reduced the active surface areas, leading to reduced extraction efficiencies. Also, the long polymerization times was produced densely packed polypyrrole particles which restricted the interactions between the target analytes and the sorbent. Consequently, 1.0 h was chosen for the polypyrrole polymerization.

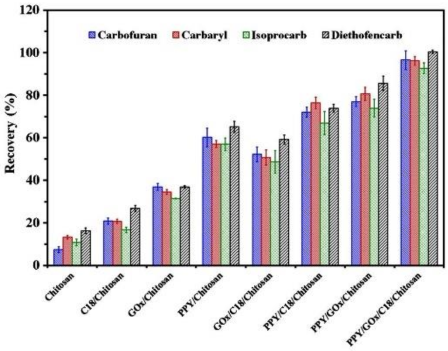

Fig. 3 Extraction efficiency of different types of sorbents for carbamate pesticides

Effect of amount of graphene oxide and C18 silica

The amount of graphene oxide in the sorbent can affect the sorbent's efficiency during the extraction of carbamate pesticides. Therefore, the graphene oxide content of a series of sorbents was varied from 0.05 to 0.3% *w*/*v* and, after extracting carbamate pesticides, the results of the extractions with these sorbents were compared. These results are shown in Fig. 4b. The recovery increased with the increment of graphene oxide concentration from 0.05 to 0.10% *w*/*v* and then remained almost constant with further increments of graphene oxide. Therefore, the concentration of graphene oxide of 0.10% *w*/*v* was chosen for further parameters. The influence of the concentration of C18-bonded silica was similarly investigated from 0.30 to 2.0% *w*/*v* (Fig. 4c). The recovery increased when the C18 silica concentration was increased from 0.30 to 1.0% *w*/*v* and then stayed almost constant. Thus, the concentration of 1.0% *w*/*v* C18 silica was selected for further experiments.

Type and volume of desorption solvent

For the SPE method, the type of desorption solvent or eluent is an important factor affecting the desorption efficiency. After consideration of the properties of the sorbent and its interactions with the target analytes, various desorption solvents were chosen for investigation. These solvents were methanol, acetone, acetonitrile, ethanol, ethyl acetate, propanol, dichloromethane, ethyl acetate + acetonitrile (1:1), ethyl acetate + methanol (1:1), dichloromethane + acetonitrile (1:1), and dichloromethane + methanol (1:1). As shown in Fig. 4d, acetonitrile provided the highest recoveries of all the analytes of interest and was hence selected as the optimum desorption solvent for the optimizations of the subsequent parameters. The influence of the desorption solvent (acetonitrile) volume was evaluated between 1.0 and 4.0 mL. As shown in ESM Fig. S3, recoveries improved as the desorption solvent's volume increased up to 3.0 mL but the further increment of the volume of acetonitrile, did not significantly increase recoveries. Therefore, 3.0 mL of acetonitrile was chosen as optimum condition.

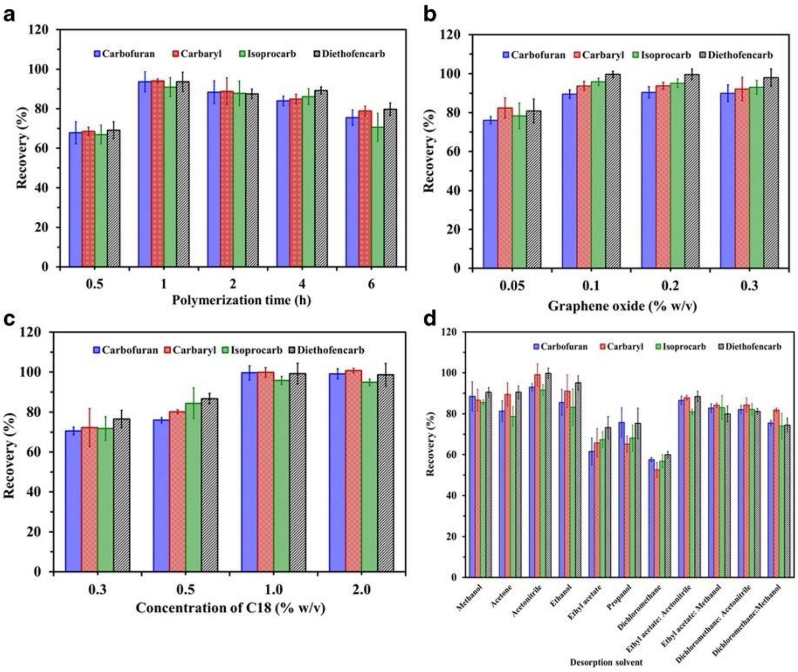

Fig. 4 Effect of polymerization time (**a**), amount of graphene oxide (**b**), concentration of C18 (**c**), and type of desorption solvent (**d**) on the extraction efficiency of carbamate pesticides using composite monolith PPY/GOx/C18/chitosan cryogel sorbent

Effect of sample volume and flow rate

In SPE procedure, the breakthrough volume is an important parameter which affects the extraction efficiency and enrichment factors of target analytes. For this work, different sample volumes were loaded through to the sorbent keeping constant the amount of pesticides. The recoveries decreased when the sample volume was greater than 20.0 mL (ESM Fig. S4). Therefore, the sample volume of 20 mL was chosen for further experiment. The effect of the sample flow rate on extraction efficiency was investigated between 0.5 and 8.0 mL min^{-1}. As shown in ESM Fig. S5, the extraction efficiency decreased when the flow rate exceeded 5.0 mL min^{-1} and therefore, 5.0 mL min^{-1} was the chosen for future experiment.

Effect of sample pH

The sample pH is an important factor in the efficient extraction and the stability of the sorbent. The effect of sample pH was investigated by varying the sample pH from 2 to 10 with HCl or NaOH. The extraction efficiencies were not significantly different when the sample pH was in the range from 2 to 8 but extraction efficiency decreased at pH 10.0 (ESM Fig. S6) due to the weak alkaline property of carbamate, which are easily hydrolyzed in strong alkaline media. However, the pH of real samples is normally lower than 8; thus, further extractions were performed without adjusting the sample pH.

Effect of ionic strength

The effect of the ionic strength of the sample solution was also investigated by adding NaCl to sample solutions in amounts of 0, 2.0, 5.0, 10.0, 15.0, and 20.0% (*w/v*). The results showed that the extraction efficiency of carbamate pesticides decreased with the increasing concentrations of NaCl (ESM Fig. S7). Therefore, the extraction of carbamate pesticides using the composite monolith PPY/GOx/C18/chitosan cryogel sorbent was performed without the addition of salt.

Analytical performances

The developed SPE sorbent was used for the extraction and pre-concentration of carbamate pesticides prior to their analysis by HPLC. The performance of the analytical method which includes linearity, limits of detection (LODs), and limits of quantification (LOQs) were evaluated. The results are shown in ESM Table S3. The method had good linearity in the range of 1.0 to 500 μg L^{-1} for carbofuran and diethofencarb, in the range of 0.5 to 500 μg L^{-1} for carbaryl, and in the range of 2.0 to 500 μg L^{-1} for isoprocarb with coefficients of determination (R^2) that ranged from 0.9993 to 1.0000. The LOD (based on signal to noise ratio of 3) was 0.5 μg L^{-1} for carbaryl, 1.0 μg L^{-1} for carbofuran and diethofencarb, and 2.0 μg L^{-1} for isoprocarb. The LOQ (based on signal to noise ratio of 10) was 4.0 μg L^{-1} for carbofuran and diethofencarb, 1.5 μg L^{-1} for carbaryl, and 8.0 μg L^{-1} for isoprocarb.

Real sample analysis

The developed sorbent was applied for the determination of carbamate pesticides in orange, grape, apple, pomegranate, and tomato juices. The analysis detected low concentrations of carbofuran in the pomegranate and tomato juices, while carbaryl and isoprocarb were also detected in the tomato juice (ESM Table S4). The accuracy of the developed sorbent was also evaluated by spiking standard carbamate pesticides in fruit juice at concentrations of 10, 50, and 100 μg L^{-1}. As shown in ESM Table S5, the developed sorbent obtained satisfactory recoveries in the range of 84.1 to 99.5%. Figure 5 shows typical chromatograms of a juice sample and a juice sample spiked at 10.0 μg L^{-1}.

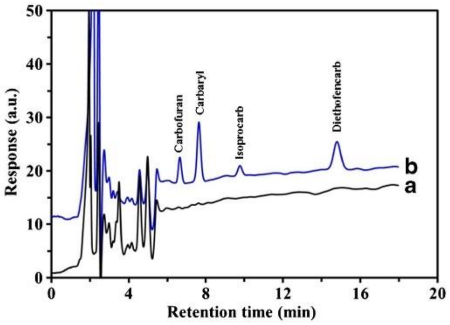

Fig. 5 Typical HPLC chromatograms of grape juice sample (a) and grape juice sample spiked at 10 μg L^{-1} (b) after extraction using composite monolith PPY/GOx/C18/chitosan cryogel sorbent

Reproducibility and reusability

The reproducibility of the prepared sorbent was evaluated by comparing the extraction efficiency of six different lots prepared at different times under the same conditions. The developed composite monolith sorbents produced a relative standard deviation lower than 10% (ESM Fig. S8), which indicated that the sorbent preparation had good reproducibility. The developed sorbent was also evaluated for reusability in the extraction of carbamate pesticides in fruit juices. After the first use, the sorbent was washed with 2.0 mL of acetonitrile and the carry-over was assessed by the determination of carbamate pesticides in the washing solvent. When no carbamate pesticide signal was detected, the developed sorbent was used for the next extraction. The results show that the extraction efficiency did not significantly change after 13 adsorption cycles and was still higher than 80% (ESM Fig. S9). The slight decrease in efficiency thereafter was possibly due to the persistence of interferences from the real samples on the active sorbent surfaces. Interferences of this type would hinder the interactions between the carbamate pesticides and the sorbent. These results show that the developed composite monolith PPY/GOx/C18/chitosan cryogel sorbent has good physical and chemical stability and can be reused up to 13 times, which would help to reduce sorbent preparation time and analysis cost.

Comparison between the composite monolith PPY/GOx/C18/chitosan cryogel sorbent and commercial sorbent

The extraction efficiency of the developed composite monolith PPY/GOx/C18/chitosan cryogel sorbent was compared with a commercial (C18) sorbent for the determination of carbamate pesticides. As shown in ESM Fig. S10, the developed sorbent produced a higher recovery than the commercial SPE sorbent. The reason for this greater efficiency may be the integration of polypyrrole, octadecyl silica, and graphene oxide. These components can increase the number of the adsorption sites at which carbamate pesticides can be adsorbed through hydrophobic interaction with octadecyl silica, hydrogen bonding, and π-πinteraction with polypyrrole and graphene oxide. Further advantages of the composite monolith PPY/GOx/C18/chitosan cryogel sorbent are exhibited low back pressure and can be reused.

Comparison with other methods

The developed method was compared with methods developed in other previous works (Table 1). The extraction efficiency and repeatability of the developed sorbent are better than or comparable to sorbents reported in other works. The detection limit obtained in this work is sufficient for the analysis of trace

Table 1 Comparison of the developed method with previous reported methods of carbamate pesticides analysis

Analytical methods	Sample preparation method	Pesticides	Sample amount	LOD (μg L^{-1} or μg kg^{-1})	Recovery (%)	RSD (%)	Reference
UHPLC-MS/MS	G-PT/SPE	Isoprocarb, diethofencarb	3 mL (fruit juice)	0.020–0.033	90–125	< 5	[5]
HPLC-MS/MS	MASE/SPE	Carbofuran, carbaryl, isoprocarb	10 g (rice)	1.17–4.40	66–103	< 9	[32]
HPLC-DAD	G-MNPs/MSPE	Carbofuran, isoprocarb	10 mL (tomato)	1.8–2.1	90–109	< 6	[33]
HPLC-UV	MPC/MSPE	Carbaryl, isoprocarb	50 mL (apple)	0.1–0.2	89–110	4–5	[34]
HPLC-DAD	Graphene-modified TiO_2 nanotube	Carbaryl, isoprocarb, diethofencarb	10 mL (water)	2.27–3.26	84–109	2–7	[6]
HPLC-DAD	G-HF/LPME	Carbaryl, isoprocarb, diethofencarb	20 g (fruit)	0.2–1.0	89–107	6–8	[7]
UPLC–MS/MS	SPE (GO)	Carbaryl, isoprocarb, diethofencarb	50 mL (water)	0.001–0.005	81–111	< 6	[35]
HPLC-DAD	MSA/DLLME	Carbofuran, carbaryl, isoprocarb	5 mL (tea)	0.13–0.61	79–114	4–8	[20]
HPLC-DAD	PPY/GOx/C18/chitosan cryogel/SPE	Carbofuran, carbaryl, isoprocarb, diethofencarb	20 mL (fruit juice)	0.5–2.0	84–98	< 6	This work

G-PT graphene pipette tip, *SPE* solid-phase extraction, *MASE* microwave-assisted water steam extraction, *G-MNPs* graphene-based magnetic nanoparticles, *MSPE* magnetic solid-phase extraction, *MPC* magnetic Fe_3O_4-doped porous carbon, *G-HF* graphene reinforced hollow fiber, *LPME* liquid-phase microextraction, *MSA* magnetic stirring-assisted, *DLLME* dispersive liquid–liquid microextraction

carbamate pesticides in fruit juices. Therefore, the developed composite monolith PPY/GOx/C18/chitosan cryogel sorbent can be used as an alternative simple and rapid sorbent for the extraction and enrichment of carbamate pesticides in fruit juices.

Conclusions

A hierarchical porous composite monolith PPY/GOx/C18/chitosan cryogel sorbent was developed and used as an effective SPE sorbent for the extraction and pre-concentration of carbamate pesticides. The developed sorbent showed a high porosity and low back pressure which enabled its use at high flow rates during sample loading. Applied for the pre-concentration of carbamate pesticides from fruit juices, the optimized sorbent material showed recoveries in the range of 84.1 to 99.5%. The pre-concentration and clean-up procedures are performed in one single step. In addition, the composite monolith PPY/GOx/C18/chitosan cryogel sorbent has good physical and chemical stability and can be reused up to 13 times, which helps to reduce analysis cost and saves time.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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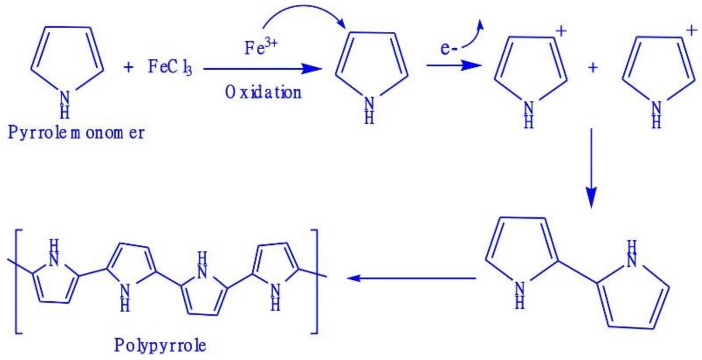
Analytical and Bioanalytical Chemistry

Electronic Supplementary Material

A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices

Pattamaporn Klongklaew, Thamolwan Naksena, Proespichaya Kanatharana, Opas Bunkoed



Scheme S1 Reaction mechanism of polypyrrole

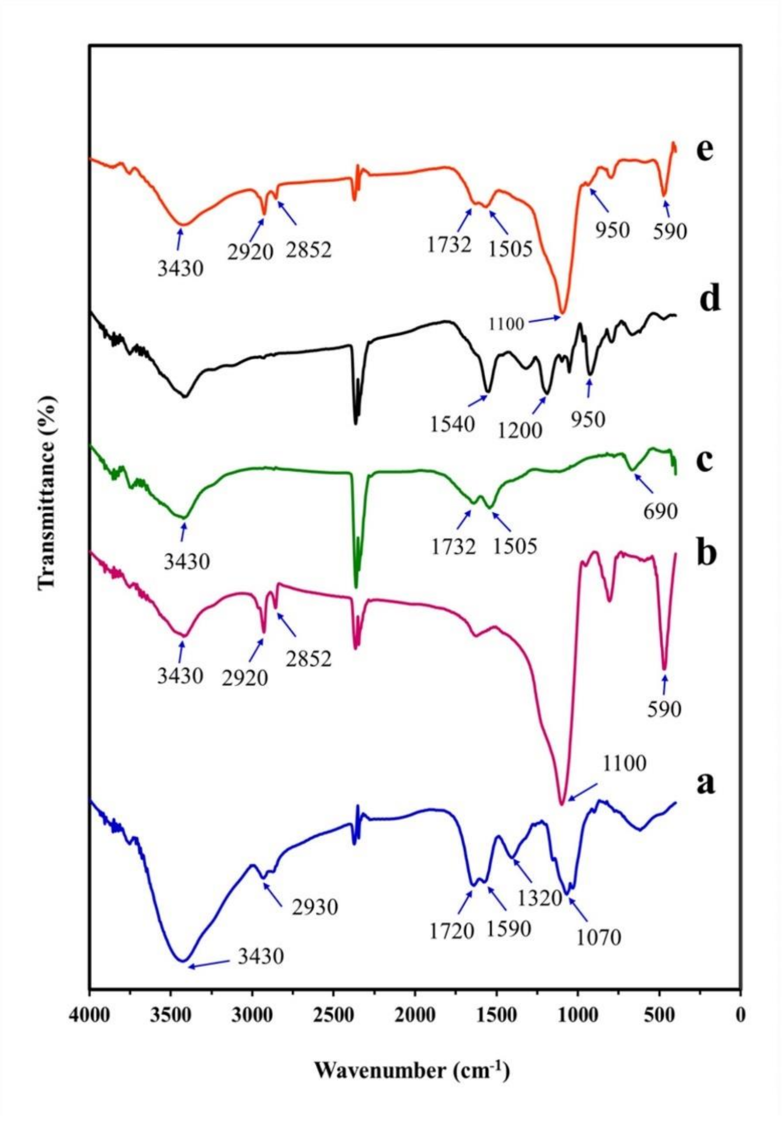


Fig. S1 FT-IR spectra of chitosan (a), SiO_2-C18 (b), graphene oxide (c), polypyrrole (d) and composite monolith PPY/GOx/C18/Chitosan cryogel sorbent (e)

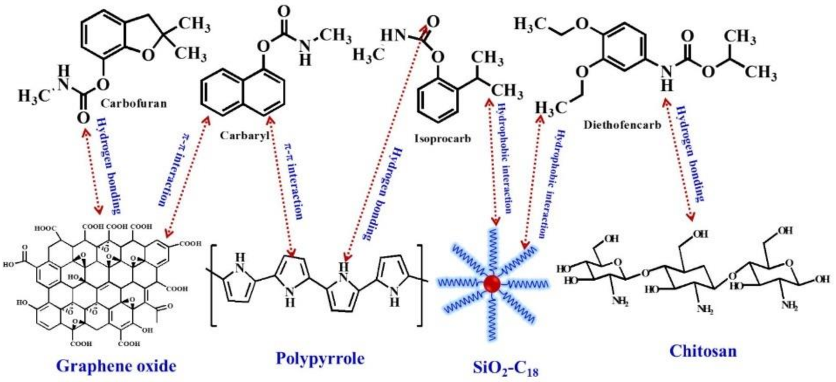


Fig. S2 The interactions between the composite monolith PPY/GOx/C18/Chitosan cryogel sorbent and carbamate pesticides

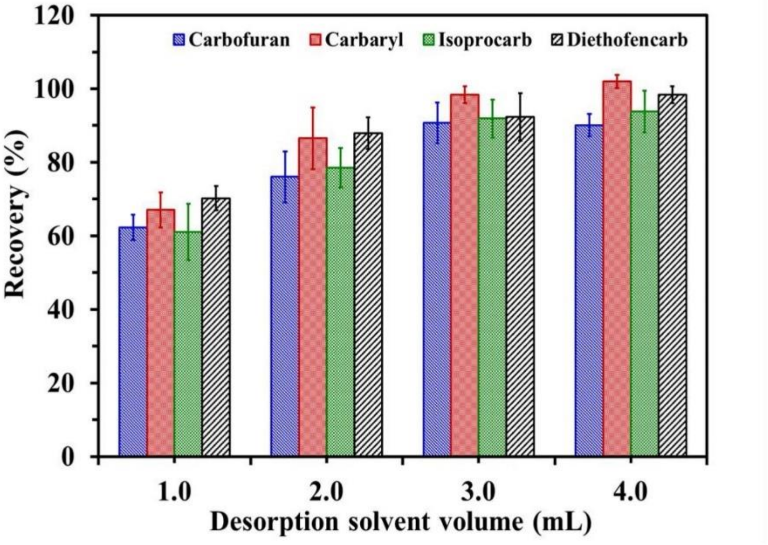


Fig. S3 Effect of desorption solvent volume on the extraction efficiency of carbamate pesticides using composite PPY/GOx/C18/Chitosan cryogel sorbent

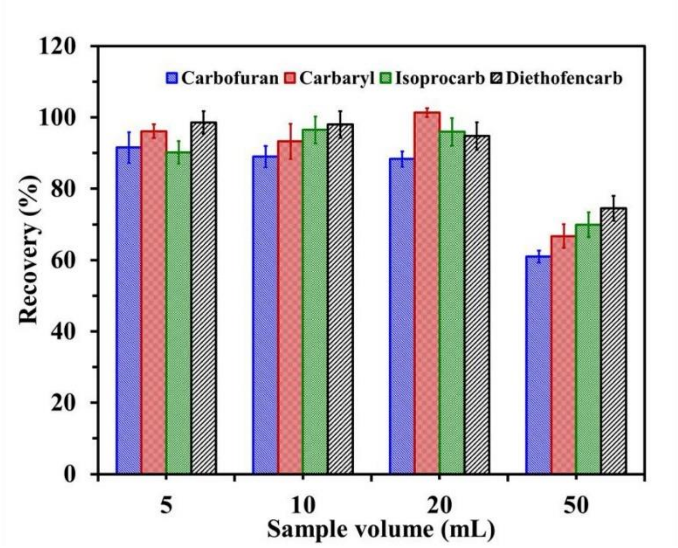


Fig. S4 Effect of sample volume on the extraction efficiency of carbamate pesticides using composite PPY/GOx/C18/Chitosan cryogel sorbent

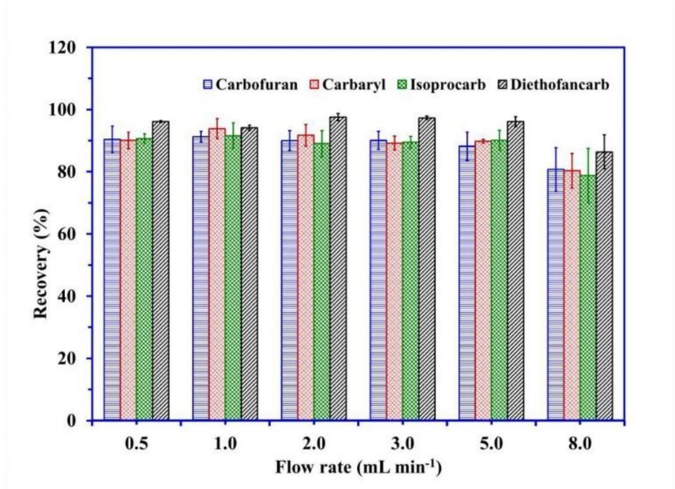


Fig. S5 Effect of sample flow rate on the extraction efficiency of carbamate pesticides using composite PPY/GOx/C18/Chitosan cryogel sorbent

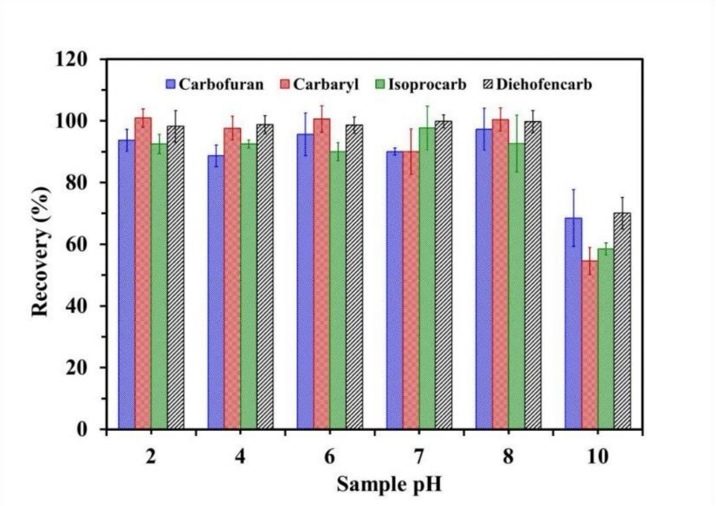


Fig. S6 Effect of sample pH on the extraction efficiency of carbamate pesticides using composite monolith PPY/GOx/C18/Chitosan cryogel sorbent

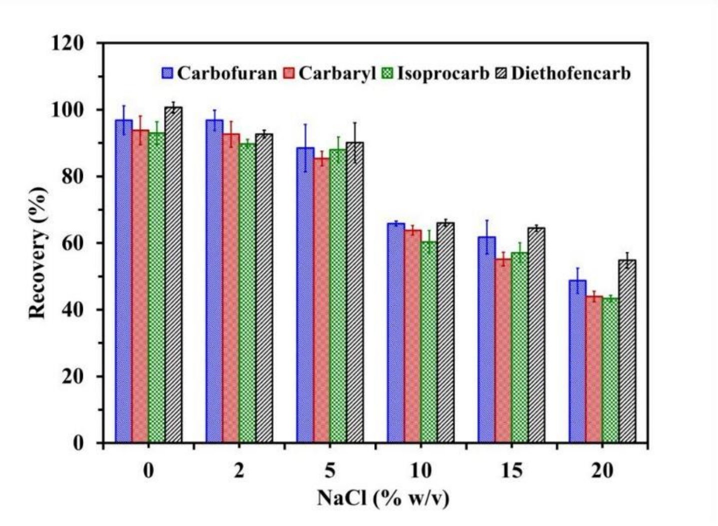


Fig. S7 Effect of ionic strength on the extraction efficiency of carbamate pesticides using composite monolith PPY/GOx/C18/Chitosan cryogel sorbent

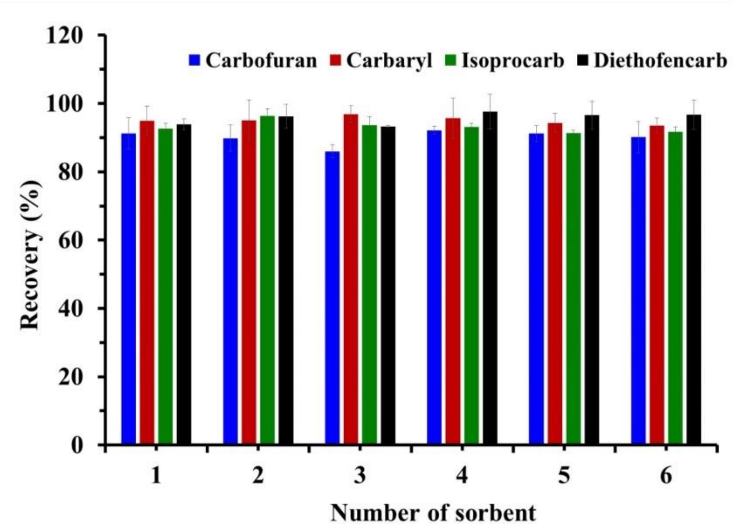


Fig. S8 The reproducibility of the composite monolith PPY/GOx/C18/Chitosan cryogel sorbent for the determination of carbamate pesticides

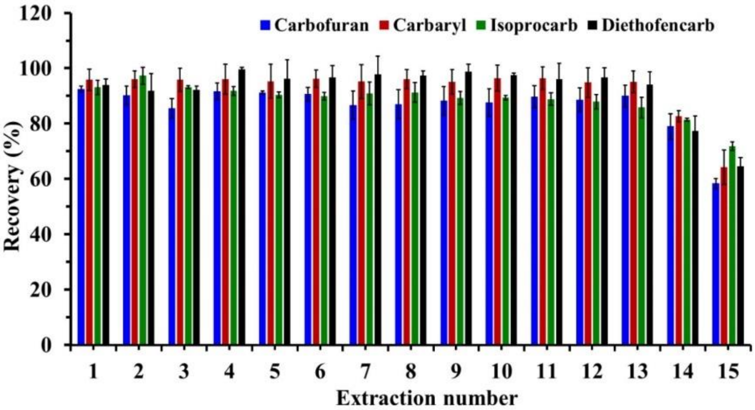


Fig. S9 The reusability of the composite monolith PPY/GOx/C18/Chitosan cryogel sorbent for the determination of carbamate pesticides

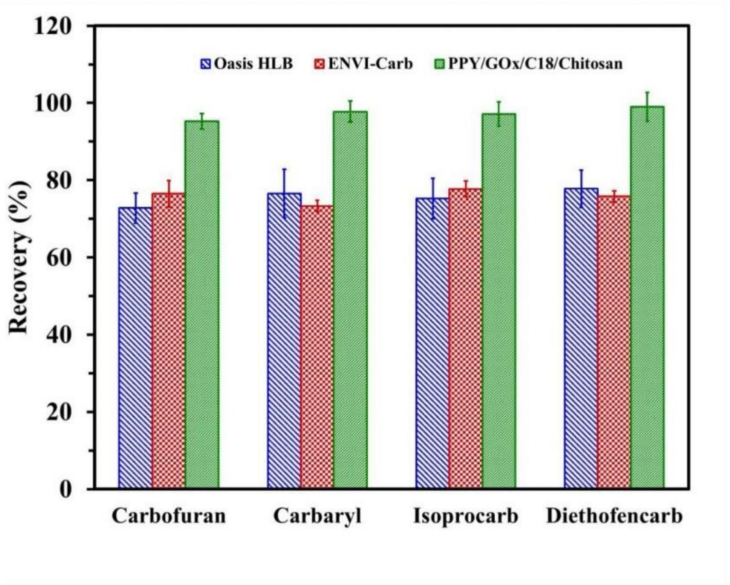


Fig. S10 Comparison of the extraction efficiency of the composite monolith PPY/GOx/C18/Chitosan cryogel sorbent and commercial sorbent (Oasis HLB and ENVI-Carb)

Table S1 The chemical composition of different adsorbent

Type of sorbent	Chitosan	Graphene oxide	C18	Polymerization time of polypyrrole
Chitosan	2.0 % w/v	–	–	–
C18/Chitosan	2.0 % w/v	–	1.0 g	–
GOx/Chitosan	2.0 % w/v	0.10 g	–	–
PPY/Chitosan	2.0 % w/v	–	–	1 h
GOx/C18/Chitosan	2.0 % w/v	0.10 g	1.0 g	–
PPY/C18/Chitosan	2.0 % w/v	–	1.0 g	1 h
PPY/GOx/Chitosan	2.0 % w/v	0.10 g	–	1 h
PPY/GOx/C18/Chitosan	2.0 % w/v	0.10 g	1.0 g	1 h

Table S2 The BET surface areas and extraction recovery of different types of monolith sorbents for the determination of carbamate pesticides

Type of sorbent	BET surface areas ($m^2 g^{-1}$)	Recovery (%) ± SD			
		Carbofuran	Carbaryl	Isoprocarb	Diethofencarb
Chitosan	0.57	7.4±1.3	13.3±0.8	10.8±1.6	16.4±1.3
C18/Chitosan	1.80	20.9±1.5	20.8±1.1	16.8±1.3	26.9±1.4
GOx/Chitosan	5.03	36.9±1.6	34.6±1.1	31.6±0.1	36.9±0.6
PPY/Chitosan	15.01	60.1±4.3	57.0±1.6	56.9±3.1	65.0±2.6
GOx/C18/Chitosan	8.10	52.1±3.5	50.7±3.6	48.6±5.3	59.1±2.2
PPY/C18/Chitosan	18.40	72.0±2.3	76.4±2.7	66.8±5.5	73.9±1.9
PPY/GOx/Chitosan	20.40	77.0±2.3	80.6±3.1	73.9±4.1	85.6±3.3
PPY/GOx/C18/Chitosan	24.27	96.5±4.4	96.1±1.9	92.6±2.5	100.3±0.8

Table S3 The analytical performance of the composite monolith PPY/GOx/C18/Chitosan cryogel sorbent coupled with HPLC for the analysis of carbamate pesticides

Pesticides	Linearity ($\mu g L^{-1}$)	Regression linear equation	R^2	LOD ($\mu g L^{-1}$)	LOQ ($\mu g L^{-1}$)
Carbofuran	1.0 – 500	$y = (0.1521\pm0.0029)x + (0.50\pm0.84)$	0.9993	1.0	4.0
Carbaryl	0.5 – 500	$y = (0.3390\pm0.0019)x - (0.05\pm0.45)$	0.9999	0.5	1.5
Isoprocarb	2.0 – 500	$y = (0.0590\pm0.0001)x + (0.314\pm0.038)$	1.0000	2.0	8.0
Diethofencarb	1.0 – 500	$y = (0.1752\pm0.0011)x - (0.38\pm0.32)$	0.9999	1.0	4.0

Table S4 Concentration of carbamate pesticides in fruit juice samples

Juice Samples	Concentration ($\mu g\ L^{-1}$)			
	Carbofuran	Carbaryl	Isoprocarb	Diethofencarb
Orange	N.D.	N.D.	N.D.	N.D.
Grape	N.D.	N.D.	N.D.	N.D.
Apple	N.D.	N.D.	N.D.	N.D.
Pomegranate	8.57±0.69	N.D.	N.D.	N.D.
Tomato	< LOQ	3.85±0.13	< LOQ	N.D.

N.D. = Not detectable

Table S5 Recovery of carbamate pesticides in spiked fruit juice

Juice samples	Spiked concentration ($\mu g\ L^{-1}$)	Recovery ± SD (%)			
		Carbofuran	Carbaryl	Isoprocarb	Diethofencarb
Orange	10	97.8±1.6	97.5±0.9	93.8±4.8	92.2±1.8
	50	92.7±1.6	94.3±4.6	91.6±5.6	96.2±3.1
	100	97.2±4.4	94.4±0.5	88.5±0.8	98.1±2.4
Grape	10	84.6±2.3	99.5±0.9	84.7±2.3	86.1±1.4
	50	90.8±3.4	84.1±1.5	84.9±0.4	96.2±5.4
	100	93.8±5.3	98.5±3.3	87.6±2.2	92.9±4.5
Apple	10	84.2±2.6	96.3±1.0	86.0±1.9	95.3±3.2
	50	85.1±1.2	84.4±1.1	94.6±1.2	97.1±1.1
	100	85.7±4.8	89.1±1.8	90.7±1.4	94.8±1.6
Pomegranate	10	86.9±2.8	91.0±1.5	90.4±1.1	93.5±0.8
	50	86.1±0.8	89.2±1.5	85.1±2.1	96.2±1.3
	100	86.9±0.4	86.1±4.3	94.8±0.4	86.3±0.4
Tomato	10	85.6±5.7	87.4±3.8	89.4±0.9	95.8±1.7
	50	86.0±4.4	85.2±0.8	86.3±4.1	89.8±0.8
	100	88.9±1.1	86.8±4.8	87.3±0.8	86.1±0.9

Paper II

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Development of doubly porous composite adsorbent for the extraction of fluoroquinolones from food samples

Pattamaporn Klongklaew, Proespichaya Kanatharana, Opas Bunkoed*

Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

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ABSTRACT

A doubly porous microcomposite polyaniline/graphene oxide/octadecyl-bonded silica magnetite (PANI/GOx/C18-SiO_2-Fe_3O_4) alginate adsorbent was developed and employed to extract fluoroquinolones. The Fe_3O_4 facilitated rapid and convenient for the separation of the adsorbent from sample solutions. The double porosity of the alginate hydrogel enhanced the surface area of the polyaniline coating. The developed method exhibited good linearity of 0.0010–50 $\mu g\,L^{-1}$ for danofloxacin; 0.0050–50 $\mu g\,L^{-1}$ for norfloxacin, ciprofloxacin and enrofloxacin; and 0.010–50 $\mu g\,L^{-1}$ for sarafloxacin and difloxacin. The limits of detection were between 0.001 and 0.010 $\mu g\,L^{-1}$ with RSD below 9.0%. The PANI/GOx/C18-SiO_2-Fe_3O_4 adsorbent was utilized to extract fluoroquinolones from honey, milk and egg samples and satisfactory extraction recoveries were achieved ranged from 80 to 98%. The developed adsorbent has good stability which can be reused up to 7 times, is simple to prepare and convenient to use for the extraction fluoroquinolones.

1. Introduction

Fluoroquinolones (FQs) are extensively used in veterinary medicine (Speltini et al., 2015) and as feed additives due to their broad-spectrum antibacterial activity (Benito-Peña, Urraca, Sellergren, & Moreno-Bondi, 2008), good oral absorption and tissue penetration rates. Because FQs biodegrade poorly and are not fully metabolized in the body, they pass into the environment (Tian et al., 2014; He et al., 2017). Since residual quantities often persist in foodstuffs and edible tissues, FQs also enter the food chain (Sun et al., 2016). Continuous exposure to antibiotics, even at low concentrations, might produce resistant bacteria (Deng et al., 2017). In addition, the side effects of fluoroquinolone antibiotics include tendon disorders, hepatotoxicity, and disturbances of the central nervous system and gastrointestinal tract (He et al., 2017). Thus, the European Union set the maximum residue limits (MRLs) of sarafloxacin in chicken at 10 $\mu g\,kg^{-1}$ and of ciprofloxacin in meat or milk at 100 $\mu g\,kg^{-1}$. Consequently, fast, convenient and reliable methods for the monitoring of fluoroquinolones have been developed. Liquid chromatography has normally been utilized for the monitoring of fluoroquinolones because it is a sensitive and precise technique (Aufartová et al., 2017). However, because the concentration of fluoroquinolones in real samples is relatively low and various matric interferences may present, an appropriate sample pretreatment procedure is normally needed before instrumental determination.

Reported extraction and pretreatment strategies for FQs determination include liquid phase extraction (LE) (Huet et al., 2006), solid phase extraction (SPE) (Wang, Yuan, Yang, Han, & Yan, 2015), matrix solid phase dispersion (MSPD) (He et al., 2017), solid phase micro-extraction (SPME) (Mitani & Kataoka, 2006; Liu et al., 2012), dispersive liquid–liquid micro-extraction (DLLME) (H. Wang et al., 2016), supercritical fluid extraction (SFE) (Shen et al., 2004), electrical field assisted dispersion (Silva, Orlando, & Faria, 2016), salting-out assisted liquid–liquid extraction (Xia, Yang, & Liu, 2012) and microwave extraction (Aufartová et al., 2017). SPE is the most extensively used because of its high extraction recovery and preconcentration factor. However, the conventional SPE adsorbent is expensive and tedious to use. Recently, magnetic solid phase extraction (MSPE) has become a favored method of extracting analytes from sample solution. Using an external magnet, separating the adsorbent from the sample solution is simple and easy (Bunkoed & Kanatharana, 2015; Kaewsuwan, Kanatharana, & Bunkoed, 2017). In addition, magnetic adsorbents can be reused after washing with the appropriate solution (Anirudhan, Christa, & Deepa, 2017; Ji et al., 2017).

However, naked magnetite nanoparticles (Fe_3O_4) are not selective towards complex matrices, prone to oxidation at low pH and tend to aggregate. To improve adsorption, the magnetite nanoparticles have been functionalized with highly specific ligands or composited with high-affinity materials (Ji et al., 2017; Liu, Liao, & Huang, 2017). In this

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* Corresponding author.
E-mail addresses: proespichaya.K@psu.ac.th (P. Kanatharana), opas.b@psu.ac.th (O. Bunkoed).

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work, a hybrid microcomposite adsorbent of polyaniline/graphene oxide/C18-SiO_2-Fe_3O_4 alginate hydrogel was developed for the extraction of fluoroquinolones. The graphene oxide and C18-SiO_2-Fe_3O_4 magnetic nanoparticles were entrapped in an alginate hydrogel to form a microcomposite adsorbent. A double micropore system was generated in the hydrogel adsorbent to increase the surface area receiving the polyaniline thin film coating. The high- affinity materials of polyaniline, graphene oxide and octadecyl adsorbed fluoroquinolones via hydrogen bonding, π-π and hydrophobic interactions. The doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel was applied to extract fluoroquinolones from food samples for detection with HPLC.

2. Experimental

2.1. Chemical and reagents

Alginic acid sodium salt, ammonium persulfate, graphene oxide powder, iron (II) chloride tetrahydrate, iron (III) chloride hexahydrate and trimethylamine were purchased from Sigma-Aldrich (Steinheim, Germany). Hydrochloric acid and aniline were from Loba Chemie (Mumbai, India). Ammonium hydroxide was from J.T. Baker (United States, USA). Octadecyl dimethyl chlorosilane and phosphoric acid were from Macron Fine Chemicals (United States, USA). Calcium chloride, calcium carbonate, acetic acid and toluene were from Merck (Darmstadt, Germany). Methanol, ethanol, dichloromethane and acetonitrile were from RCI Labscan (Bangkok, Thailand). Tetraethyl orthosilicate (TEOS), ciprofloxacin, danofloxacin, difloxacin, norfloxacin, enrofloxacin and sarafloxacin were from Tokyo Chemical Industry (Tokyo, Japan).

2.2. Instrumental and HPLC conditions

HPLC determination was performed using a Hewlett-Packard 1100 series (Agilent, Germany) with a Fortis C18 HPLC column (4.6 × 150 mm I.D., 5 μm, Fortis Technologies Ltd.). The mobile phase was 25 mM phosphoric acid (A) and acetonitrile (B). A gradient separation mode was performed as follows: 0–7 min, 18–22 %B; 7–12 min, 22 %B; 12–15 min, 22–18 %B and 15–18 min, 18 %B. The injection volume and flow rate were 20 μL and 0.9 mL min^{-1}, respectively. Fluoroquinolones were detected at 280 and 450 nm as an excitation and emission wavelengths, respectively. The surface morphology of the prepared adsorbent was characterized using a scanning electron microscope (JSM-5200, JEOL, Japan). Fluorescent Stereo Microscopy was performed with Leica M205 FCA apparatus, Leica Microsystems (Switzerland).

2.3. Preparation of doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel

The preparation procedure of the doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel is illustrated in Fig. 1A. Fe_3O_4 was synthesized according to a previous method with minor modifications (Bunkoed, Nurerk, Wannapob, & Kanatharana, 2016). Briefly, $FeCl_3 \cdot 6H_2O$ (5.0 g) and $FeCl_2 \cdot 4H_2O$ (1.6 g) were dissolved in deionized water (100 mL) and stirred at 85 °C. NH_4OH was added dropwise to the solution, which was then stirred for 1 h to produce Fe_3O_4 nanoparticles. The obtained magnetic nanoparticles were collected using magnet, washed with 50 mL of deionized water and dried at 60 °C for 12 h. The Fe_3O_4 was then coated with a silica layer in the following sol–gel process. Fe_3O_4 nanoparticles were mixed with 100 mL ethanol, 2.0 mL NH_4OH (30% v/v), tetraethyl orthosilicate (2.0 mL) and deionized water (50 mL) and stirred at 50 °C for 12 h. The synthesized SiO_2-Fe_3O_4 nanoparticles were washed with 10 mL of deionized water and dried at 50 °C for 5 h. To functionalize the SiO_2-Fe_3O_4 with C18, 3.0 g of the nanoparticles were added into100 mL toluene. A slurry formed, which was heated to a temperature of 80 °C, at which point trimethylamine (10 mL) and 1.0 mL octadecyl dimethyl chlorosilane were added. This mixture was then refluxed for 24 h. The magnetic SiO_2-Fe_3O_4 was now functionalized with C18 and they were washed twice with 10 mL of ethanol and deionized water and dried at 50 °C for 5 h.

To prepare the microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel, 2.0% w/v alginic acid solution was prepared by dissolution in deionized water. Once the alginic acid was dissolved, 0.10 g of the synthesized C18- SiO_2-Fe_3O_4 nanoparticles, 0.10 g of GOx and 0.10 g of $CaCO_3$ were dispersed in alginic solution (100 mL) under ultrasonication for 30 min to obtain a homogeneous colloidal suspension.

The suspension mixture was then added dropwise to 5.0% w/w calcium chloride solution to create the microcomposite of Ca-alginate. The GOx/C18-SiO_2-Fe_3O_4 hydrogel was immersed in in $CaCl_2$ solution for 2 h to form microspheres. Then, the microspheres were soaked in 100 mL HCl solution (20% w/v) for 5 min. In this step, $CaCO_3$ in the microcomposite reacted with HCl to produce the doubly porous network (Pinsrithong & Bunkoed, 2018). The doubly porous microcomposite GOx/C18-SiO_2-Fe_3O_4/alginate hydrogel microspheres were washed with deionized water until the pH of the water was nearly neutral (6–7) and then incubated in a mixture of 10.0 mL HCl (1.0 M) and 0.3 mL of aniline for 30 min. The GOx/C18-SiO_2-Fe_3O_4 hydrogel was polymerized by the addition of 10.0 mL ammonium persulfate. After polymerization for 30 min, the obtained doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel microspheres were washed with 10 mL of methanol and then with 20 mL of deionized water.

2.4. MSPE procedure using doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel

The MSPE procedure is shown in Fig. 1B. The doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogels (0.50 g) were added into the sample solution (10.0 mL) and stirred for 20 min. Then, an external neodymium magnet (3.0 cm × 1.0 cm I.D.) was deposited at the bottom of the vial to isolate the adsorbents from the solution. The supernatant solution was decanted and the analytes were desorbed from the adsorbents using ultrasonication with a suitable desorption solvent (a mixture of acetonitrile (45%), dichloromethane (45%) and 0.10 M acetic acid (10%). The desorption solvent was evaporated and reconstituted with 1.0 mL of mobile phase and 20 Âµl were injected into the HPLC system. After washing with 2.0 mL of desorption solvent and ultrapure water, the doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel was reused.

3. Result and discussion

3.1. Characterization of the doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel adsorbent

The doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel was characterized using scanning electron microscopy (SEM), fluorescence stereo microscopy, FTIR spectroscopy and Brunauer-Emmett-Teller (BET) method. The SEM images indicated that the surface of the alginate hydrogel was smooth (Fig. 2A), while the surfaces of the microcomposite C18-SiO_2-Fe_3O_4 alginate hydrogel (Fig. 2B) and the GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel (Fig. 2C) were rougher. An SEM image of the doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel shows that the polyaniline nanoparticles were successfully coated on the surface of the doubly porous microcomposite hydrogel (Fig. 2D). The fabrication of the doubly porous hydrogel was also investigated using fluorescence stereo microscopy. A photograph of alginate hydrogel microspheres without the generated double pore network is presented in Fig. 2E. Fig. 2F presents the microspheres after the reaction of $CaCO_3$ and HCl which created the

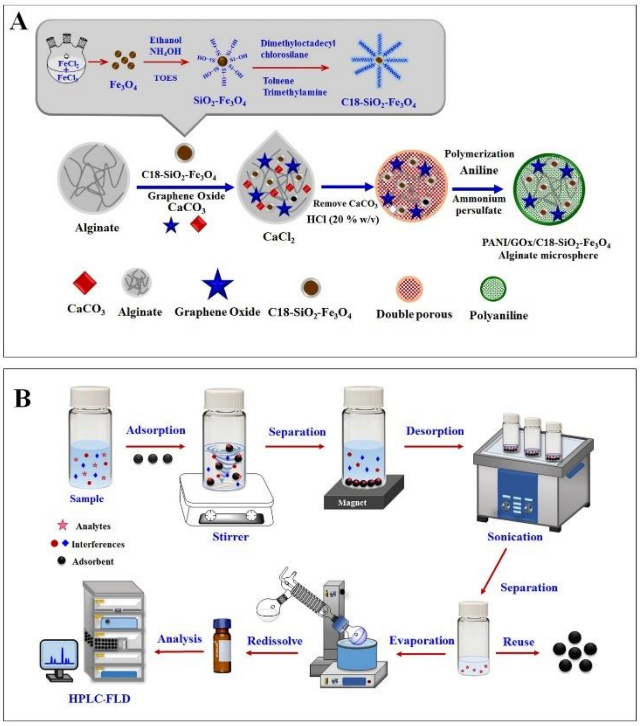

Fig. 1. The preparation procedure of a doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel (A) and the magnetic solid phase extraction procedure (B).

double pore network. Bubbles from the reaction are visible inside the hydrogel.

FTIR spectra were used to confirm the synthesis of the developed adsorbent.The absorption peaks in Fig. S1a at 1634 cm^{-1} (O=C–O asymmetric), 1414 cm^{-1} (O=C–O symmetric) and 1031 cm^{-1} (C–O) correspond to the spectrum of alginate hydrogel (Daemi & Barikani, 2012). The absorption peak of C18-SiO$_2$-Fe$_3$O$_4$ appears at 3450 cm^{-1} (–OH or Si-OH) (Fig. S1b). The peaks at 1081 cm^{-1} (Si-O-Si) and 588 cm^{-1} (Fe–O–Fe) are attributed to silica and magnetite, respectively. The characteristic peaks at 1634 cm^{-1} (C=O stretching) and 1408 cm^{-1} (C–H bending) (Fig. S1c) correspond to graphene oxide. Polyaniline (PANI) showed absorption peaks at 1630, 1401 and 1300 cm^{-1} (Fig. S1d), which were related to the C=C stretching of the quinonoid ring, benzenoid ring and C–N of aromatic ring, respectively. The FTIR spectrum of microcomposited PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate (Fig. S1e) indicated that polyaniline, graphene oxide and C18-SiO$_2$-Fe$_3$O$_4$ were successfully composited into the alginate hydrogel.

The BET surface areas of alginate/Fe$_3$O$_4$ hydrogel, doubly porous alginate/Fe$_3$O$_4$ hydrogel, doubly porous C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel, doubly porous GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel and doubly porous PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel were 4.04, 7.94, 11.23, 21.70 and 27.84 m^2 g^{-1}, respectively.

Vibrating sample magnetometry (VSM) was used to investigate the magnetic properties of PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ adsorbent. The saturation magnetization values was 8.03 emu g^{-1} (Fig. S2). The magnetic strength of the PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ adsorbent was enough for magnetic separation, and it was rapidly separated from the solution within about 3 sec using an external magnet.

3.2. *Type of adsorbents*

The fluoroquinolones extraction recoveries of the adsorbent at different stages of preparation were determined. The extraction recoveries of alginate, C18-SiO$_2$-Fe$_3$O$_4$ alginate, PANI/C18-SiO$_2$-Fe$_3$O$_4$ alginate, GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate and PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate were in the range of 12.3–17.5%, 29.1–36.4%, 50.7–55.7%, 65.8–70.6% and 88.6–92.0%, respectively (Fig. S3). The doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel provided the highest extraction recovery due to it contained more adsorption sites and more interactions could occur, including hydrogen bonding, π-π and hydrophobic interaction (Fan, He, Wu, Chen, & Hu, 2015) (Fig. S4).

3.3. *Optimization of adsorbent preparation and extraction conditions*

The parameters that might affect the extraction efficiency of the

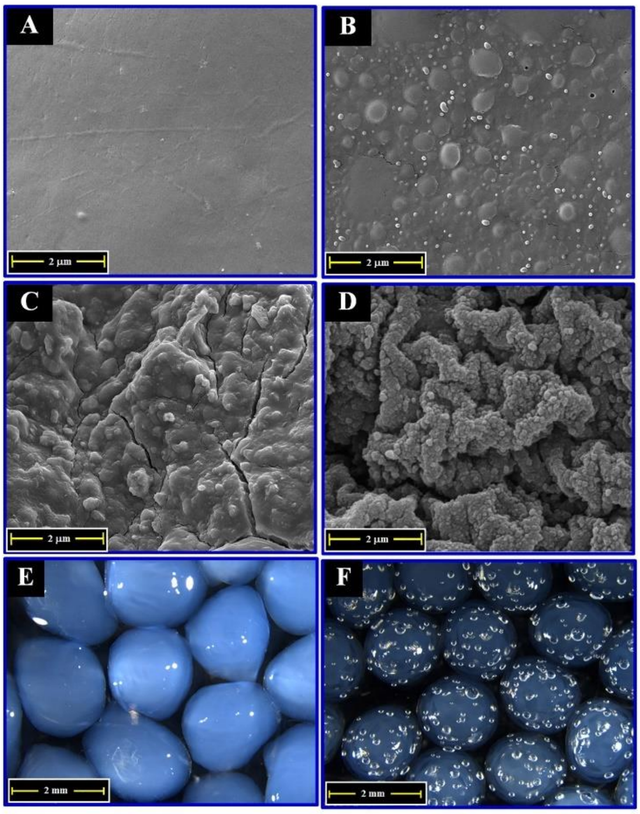

Fig. 2. SEM images of alginate hydrogel microspheres (A), Composite C18-SiO_2-Fe_3O_4 alginate hydrogel (B), Composite GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel (C) and doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel (D), Photograph of microcomposite hydrogel microspheres (E) and doubly porous microcomposite hydrogel microspheres (F).

double porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel were optimized. The optimization experiments were performed using spiked water sample and the extraction efficiency was determined in terms of extraction recovery (ER %).

$$\text{Extraction recovery}(\%\text{ER}) = (CV/C_0V_0) \times 100$$

where C is analytes concentration in the reconstituted solvent ($\mu g\ L^{-1}$), C_0 is the concentration of target analytes in spiked water ($\mu g\ L^{-1}$). V and V_0 are the volume of the reconstituted solvent and water samples (mL) respectively. Each experiment will be done in triplicate.

3.3.1. Desorption conditions

In this work, the adsorption of fluoroquinolones onto the double porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel are based on hydrogen bonding, π-π and hydrophobic interaction, different desorption solvent were investigated including methanol (MET), acetonitrile (ACN), dichloromethane (DCM), acetonitrile + dichloromethane (50:50 %v/v) and acetonitrile + dichloromethane + 0.1 M acetic acid (AC) (45:45:10 %v/v). The mixture of acetonitrile and dichloromethane in the presence of 0.1 M acetic acid provided the highest extraction recovery (Fig. 3A). This is due to under acidic condition fluoroquinolones were ionized leading to the decreasing of the interaction between the analytes and adsorbent. Therefore, a mixture of acetonitrile (45%), dichloromethane (45%) and 0.10 M acetic acid (10%) was used as the appropriate desorption solvent and its volume was also evaluated from 2.0 to 5.0 mL. The recovery increased when the desorption solvent volume increased from 2.0 to 3.0 mL and remained constant with further increments (Fig. 3B). Thus, 3.0 mL was used in subsequent experiments.

3.3.2. Effect of polymerization time of polyaniline

The polymerization time of polyaniline was optimized using durations of 15, 30 and 60 min. The extraction recovery increased with increased time of polymerization from 15 min to 30 min and it decreased after polymerization time of 60 min (Fig. 3C). Lower recovery

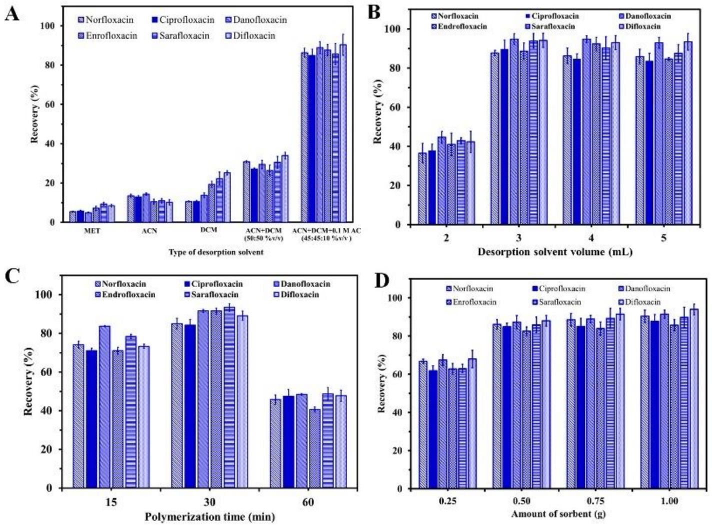

Fig. 3. Effect of type of desorption solvent (A), desorption solvent volume (B), polymerization time of polyaniline (C) and amount of adsorbent (D) on the extraction recovery of fluoroquinolones using doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel.

was obtained after shorter polymerization time (15 min) because fewer polyaniline nanoparticles were produced during that polymerization time period. Recovery decreased at 60 min polymerization time perhaps because too many polyaniline particles were present on the surfaces of the hydrogel microspheres, which reduced the active surface area of the adsorbent. Thus further polymerization of polyaniline was only performed at room temperature for 30 min.

3.3.3. Amount of adsorbent

The effect of the amount of the microcomposite adsorbent used was investigated from 0.25 g to 1.0 g. The extraction was performed using a spiked sample (10.0 mL) containing 10.0 μg L^{-1} of each of the fluoroquinolones. The extraction recovery increased as the amount of adsorbent increased from 0.25 to 0.50 g and then remained almost constant (Fig. 3D). Therefore, 0.50 g of adsorbent was chosen as the optimum amount.

3.3.4. Sample volume

Since the enrichment factor depends on the sample volume, a high sample volume provides a high enrichment factor. Too large a sample volume, however, could affect the adsorption of the analytes onto the adsorbent, which would affect extraction efficiency. Thus, different volumes of a spiked sample (10 μg L^{-1}) (5, 10, 20 mL) were investigated (Fig. 4A). The extraction recovery decreased when sample volume exceeded 10.0 mL. Thus, 10.0 mL was selected as the optimum sample volume.

3.3.5. Sample pH

Sample pH is an important factor in the adsorption of fluoroquinolones onto the adsorbent since FQs can exist in anionic, cationic and zwitterionic forms under different pH values. The sample pH was adjusted with HCl or NaOH to achieve a series of pH values of 3.0, 5.0, 7.0, 9.0 and 11.0. The sample pH of 7 provided the highest extraction recovery (Fig. 4B) because fluoroquinolones at that pH are in the zwitterionic form which has zero charge, resulting in strong hydrogen bonding between analytes and adsorbent (Malik et al., 2019). The extraction recovery decreased at pH less than 7 because fluoroquinolones under the acidic condition were ionized, so the interaction between analytes and adsorbent was reduced. Extraction recovery also decreased at pH greater than 7 due to the dissociation of the carboxylic group (anionic form), which could reduce the strength of hydrogen bonding between analytes and adsorbent surface (Malik et al., 2019). The effect of electrostatic repulsion could also reduce extraction recovery (Lian et al., 2018). Thus, the sample pH of 7 was chosen for further experiment.

3.3.6. Extraction time and stirring speed

Extraction times from 10 to 30 min were investigated. Recovery increased from 10 min up to 20 min and remained constant up to 30 min (Fig. 4C). Therefore, the 20 min was selected as optimum extraction time.

The extraction efficiency of the magnetic solid phase extraction method depends on the partition rate of the analyte from the sample solution to the adsorbent. Stirring rate is an effective way to increase the mass transfer of analytes from the solution to the adsorbent. Therefore, the effect of stirring speed on extraction was investigated from 500 rpm to 2000 rpm. As expected, extraction recovery increased as the stirring rate was increased from 500 to 1000 rpm and remained constant at higher speeds (Fig. 4D). Thus, 1000 rpm of the stirring rate was chosen as the optimum condition.

3.4. Analytical performances

Under the optimum conditions of the HPLC system and MSPE

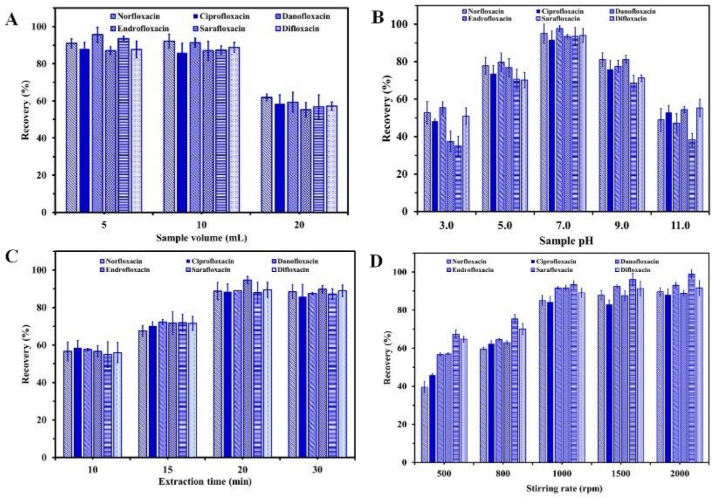

Fig. 4. Effect of sample volume (A), sample pH (B), extraction time (C) and stirring speed (D) on the extraction recovery of fluoroquinolones using doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel microspheres.

Table 1
Analytical performances of the doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel microspheres for the determination of fluoroquinolones.

Compounds	Linear range (μg L^{-1})	Regression linear equation	R^2	LOD (μg L^{-1})	LOQ (μg L^{-1})
Norfloxacin	0.0050–50	$y = 0.211x + 0.023$	0.9985	0.005	0.02
Ciprofloxacin	0.0050–50	$y = 0.261x - 0.080$	0.9983	0.005	0.02
Danofloxacin	0.0010–50	$y = 0.787x + 0.330$	0.9994	0.001	0.003
Enrofloxacin	0.0050–50	$y = 0.282x - 0.012$	0.9986	0.005	0.02
Sarafloxacin	0.010–50	$y = 0.232x + 0.031$	0.9933	0.01	0.04
Difloxacin	0.010–50	$y = 0.249x - 0.044$	0.9989	0.01	0.04

procedure. The practicality of the developed method was evaluated including the linearity, limit of detection and limit of quantification. To achieve the linearity of the method, the standard solution of fluoroquinolones at different concentration were extracted using PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ adsorbent followed by HPLC. The developed doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel provided a wide linearity from 0.001 to 50 μg L^{-1} for danofloxacin; 0.005–50 μg L^{-1} for norfloxacin, ciprofloxacin and enrofloxacin; and 0.01–50 μg L^{-1} for sarafloxacin and difloxacin (Table 1). The coefficient of determination (r^2) was better than 0.99. The LODs were within a range from 0.001 to 0.01 μg L^{-1} (S/N ≥ 3). The LOQs were in a range from 0.003 to 0.04 μg L^{-1} (S/N ≥ 10). A linear regression analysis of the calibration curve was performed using Microsoft Excel 2016 software.

3.5. Reproducibility

The reproducibility of the developed doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel microspheres was determined in terms of lot-to-lot reproducibility. Six lots (n = 6) of the microcomposite adsorbent were prepared and used to extract fluoroquinolones from spiked samples (10.0 μg L^{-1}) under the same extraction condition. The RSDs for the extraction of fluoroquinolones were in the range of 0.6–2.3% (Fig. S5). This result implied that the preparation of the double porous microcomposite adsorbent has a satisfactory reproducibility.

3.6. Reusability

The reusability of the doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel microspheres was investigated by repeated extraction of fluoroquinolones from spiked samples at 10.0 μg L^{-1}. After each use of the adsorbent, it was washed with 2.0 mL of desorption solvent and deionized water until there was no carry-over effect, before reused. Then, the same sorbent was repeatedly used for extraction of the fluoroquinolones. The developed microcomposite adsorbent can be reused up to 7 times and still maintain extraction recoveries better than 80% (Fig. S6). The reduced extraction recovery after 7 cycles may be due to loss of the polyaniline during repeated extraction and desorption steps.

3.7. Comparison of the doubly porous microcomposite adsorbent with a commercial sorbent

The performance of the doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel was compared with a C$_{18}$ packed cartridge (Oasis HLB). The results showed that both adsorbents provided acceptable extraction recovery above 80% (Fig. S7). However, the developed doubly porous microcomposite adsorbent exhibited better extraction recovery than the commercial adsorbent. This was due to the generated double porous network and integration of various materials which can enhance the adsorption ability of the microcomposite hydrogel.

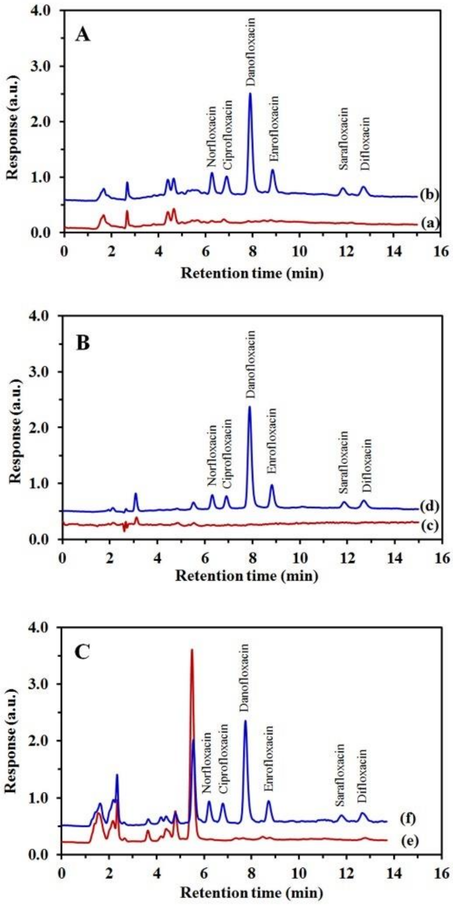

Fig. 5. HPLC chromatograms of honey (A), egg (B) and milk (C) samples with extraction using the developed double microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel adsorbent; (a) honey sample, (b) spiked honey sample, (c) egg sample, (d) spiked egg sample, (e) milk sample and (f) spiked milk sample.

3.8. Application of the developed adsorbent to real samples

The developed adsorbent was applied to determine fluoroquinolones in honey, milk and egg samples. The found concentrations are summarized in Table S1. Relatively low amounts of fluoroquinolones (much lower than the MRL values) were detected. The accuracy of the developed method was reported in terms of relative recovery (% RR), arrived at by spiking standard fluoroquinolones into real samples at 0.10, 0.50, 1.0, and 10.0 $\mu g\, kg^{-1}$. The spiked samples were extracted and determined under the optimum conditions. Satisfactory relative recoveries were achieved in the range of 80–98% (Table S2). These results indicate that the developed doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel is efficient enough to be used for the extraction of fluoroquinolones in various food samples. HPLC chromatograms of milk sample and spiked milk sample (1.0 $\mu g\, kg^{-1}$) with extraction using doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel adsorbent are showed in Fig. 5.

3.9. Comparison with other methods

The analytical performances of double porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel adsorbent was compared with other methods (Table S3). The developed method produced LODs much lower than those reported in other works (Mirzajani & Kardani, 2016; Manbohi & Ahmadi, 2015; de Oliveira et al., 2016; Wang, Yang, Liu, Feng, & Wang, 2016; He et al., 2017; Urraca, Castellari, Barrios, & Moreno-Bondi, 2014; He & Blaney, 2015; Fan et al., 2015; Gao et al., 2015). Recoveries were better than (de Oliveira et al., 2016; Urraca et al., 2014) or comparable with recoveries from some other works. The precision (% RSD) was also acceptable and comparable with other previous works. In addition, the PANI/GOx/C18-SiO_2-Fe_3O_4 adsorbent can be reused for 7 cycles which reduces the analysis costs. These results implied that the developed PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel can be used as an effective adsorbent for the extraction of fluoroquinolones in food samples.

4. Conclusion

A doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel was successfully developed and utilized as MSPE adsorbent for the extraction of fluoroquinolones in food samples. The formation of a double pore network in the microcomposite hydrogel increased the surface area of the sorbent available for the coating of polyaniline thin film. The incorporation of hydrophobic octadecyl and graphene oxide in the hydrogel and the coating of polyaniline film increased the number of available adsorption sites for fluoroquinolones. Satisfactory extraction efficiency (80–98%) was obtained with low limits of detection and good precision. The developed adsorbent has a good chemical stability and can be reused at least 7 times. In addition, the developed doubly porous microcomposite MSPE adsorbent is simple to prepare, easy to use, convenient to use and cost-effective. This developed robust microcomposite adsorbent can be modified with different high-affinity materials to extract other toxic compounds in various sample matrices.

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.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodchem.2019.125685.

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Supplementary material

Development of doubly porous composite adsorbent for the extraction of fluoroquinolones from food samples

Pattamaporn Klongklaew[1], Proespichaya Kanatharana[1], Opas Bunkoed[1]*

[1]Center of Excellence for Innovation in Chemistry, Department of Chemistry, Faculty of Science, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

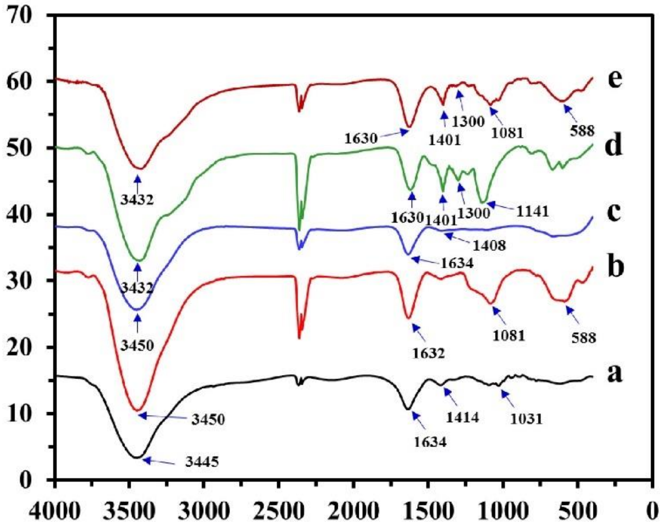

Fig. S1 FTIR spectra of alginate hydrogel (a), C18-SiO_2-Fe_3O_4 (b), graphene oxide (c), polyaniline (d) and PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel (e).

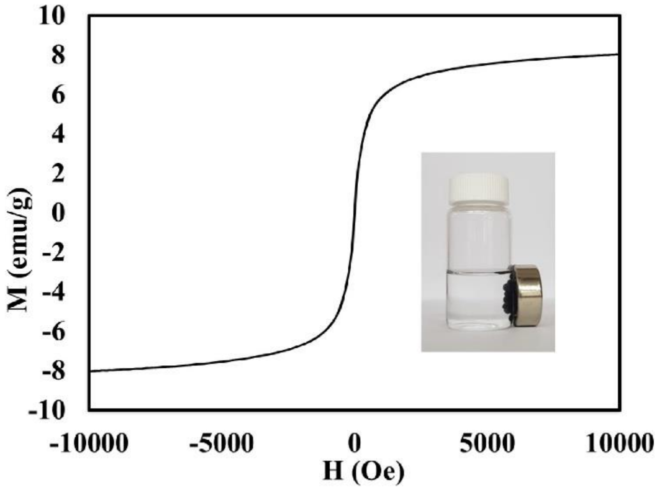

Fig. S2 Magnetization curve of PANI/GOx/C18-SiO_2-Fe_3O_4 adsorbent, the inset represents the adsorbent separated by a magnet

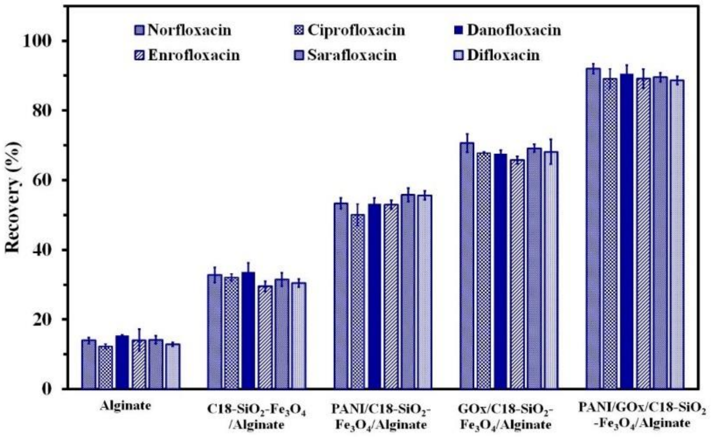

Fig. S3 Effect of type of adsorbent on the extraction recovery of fluoroquinolones.

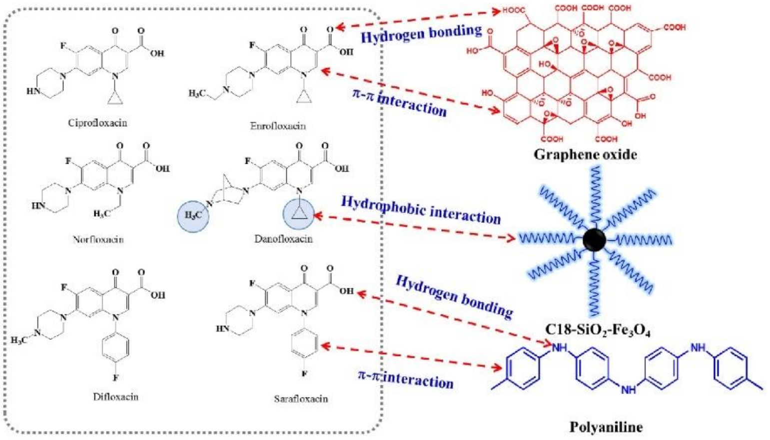

Fig. S4 The interactions between the doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel and fluoroquinolones

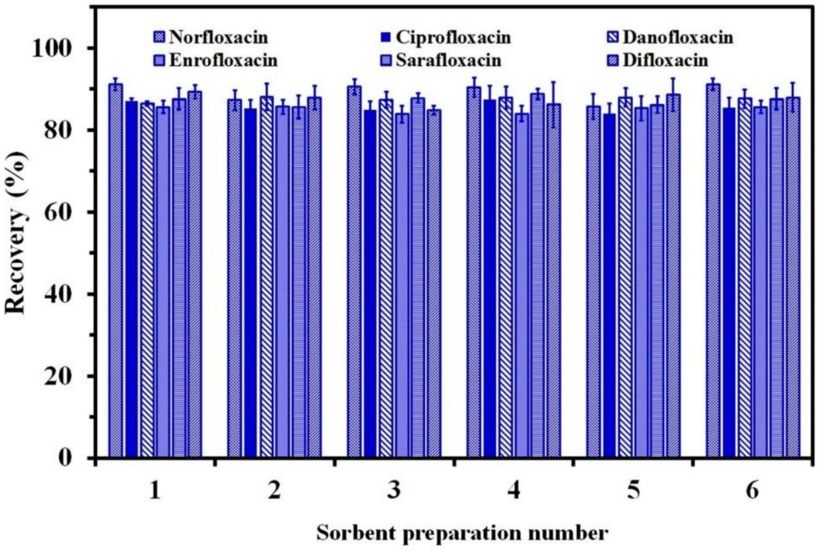

Fig. S5 The reproducibility for the preparation of doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel microspheres

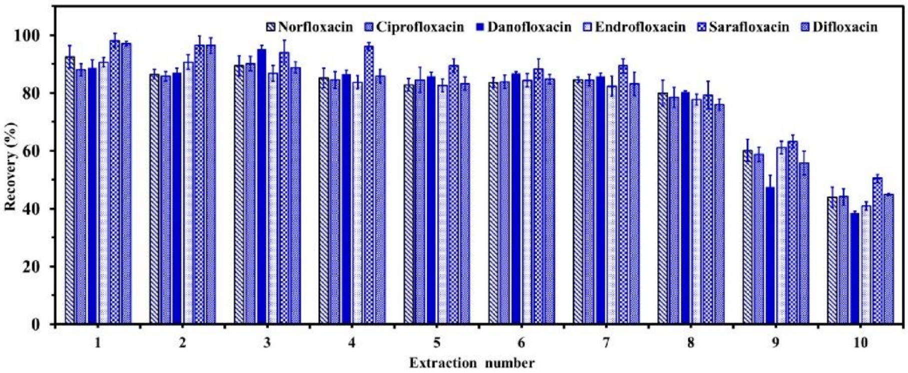

Fig. S6 Reusability of doubly porous microcomposite PANI/GOx/C18-SiO_2-Fe_3O_4 alginate hydrogel microspheres for the extraction of fluoroquinolones.

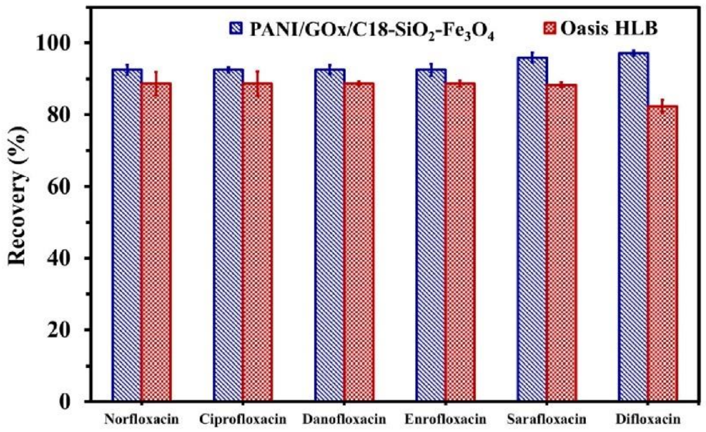

Fig. S7 The extraction efficiency of the developed doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel and commercial Oasis HLB sorbent.

Table S1 Detected concentrations of fluoroquinolones in honey, milk, and egg samples using PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ adsorbent coupled with HPLC-FLD (n=3)

sample	Concentration (μg kg^{-1})±SD					
	Norfloxacin	Ciprofloxacin	Danofloxacin	Enrofloxacin	Sarafloxacin	Difloxacin
Honey 1	0.213±0.009	0.105±0.014	0.169±0.007	2.14±0.19	0.18±0.06	0.21±0.02
Honey 2	0.269±0.004	0.146±0.004	0.260±0.003	3.33±0.07	0.28±0.02	ND
Milk 1	ND	0.172±0.013	0.070±0.021	0.76±0.03	0.54±0.02	0.14±0.05
Milk 2	ND	0.129±0.004	0.115±0.001	0.12±0.07	0.43±0.11	ND
Milk 3	ND	0.221±0.009	<LOQ	2.59±0.16	0.61±0.02	ND
Egg 1	<LOQ	0.068±0.007	<LOQ	2.05±0.08	ND	ND
Egg 2	ND	ND	ND	ND	ND	ND
Egg 3	0.240±0.002	0.058±0.005	0.008±0.001	1.72±0.11	ND	0.47±0.02

ND = Not detectable; <LOQ= lower than limit of quantification

Table S2 The analysis of fluoroquinolones in spiked food samples using doubly porous microcomposite PANI/GOx/C18-SiO$_2$-Fe$_3$O$_4$ alginate hydrogel microspheres (n=3)

Samples	Added (μg kg^{-1})	Recovery (%) ±SD					
		Norfloxacin	Ciprofloxacin	Danofloxacin	Enrofloxacin	Sarafloxacin	Difloxacin
Honey1	0.10	89.8±5.7	85.7±5.8	85.2±4.7	84.0±5.0	86.8±3.4	87.9±4.8
	0.50	84.9±1.4	83.6±3.9	86.2±5.4	83.2±3.9	85.4±3.3	90.5±4.2
	1.0	85.0±3.7	85.5±4.2	83.4±3.8	82.9±3.7	84.8±3.9	84.9±3.6
	10.0	82.0±1.8	82.9±2.4	98.2±1.7	83.8±2.5	83.0±1.9	84.8±1.5
Honey2	0.10	85.3±5.7	86.5 ±5.3	86.3±5.2	85.6±6.1	86.8±2.5	89.0±6.7
	0.50	86.1±5.9	81.2±1.4	84.0±3.9	82.6±2.7	84.2±5.3	92.4±7.3
	1.0	83.1±3.0	81.7±1.0	82.8±2.7	83.3±0.8	84.1±1.6	83.1±3.1
	10.0	84.1±3.1	86.0±3.1	83.3±1.7	84.3±0.9	81.7±0.6	81.3±0.5
Milk1	0.10	87.8±5.3	86.3±8.1	82.4±2.6	84.2±5.0	85.7±6.5	91.3±4.2
	0.50	86.1±2.1	88.0±2.7	82.6±4.1	83.5±2.3	88.0±2.2	84.0±2.1
	1.0	83.0±2.3	85.2±1.6	89.1±7.1	82.4±2.3	84.1±3.1	82.6±3.1
	10.0	81.1±0.3	82.6±0.8	83.4±3.5	81.9±1.4	85.7±2.9	83.5±1.8
Milk2	0.10	87.6±6.0	88.9±5.7	86.9±2.2	87.9±8.0	89.3±7.7	88.8±4.1
	0.50	84.9±4.6	89.4±5.0	82.7±2.8	86.8±7.8	90.0±4.3	87.8±4.6
	1.0	83.7±3.9	85.2±4.1	82.9±2.2	86.8±3.4	82.4±2.5	87.3±1.3
	10.0	83.4±1.2	81.9±0.7	87.9±2.7	82.0±0.8	83.8±2.0	83.4±2.0
Milk3	0.10	90.9±7.6	88.1±6.1	88.4±2.3	88.3±5.1	86.4±7.2	85.6±3.5
	0.50	89.0±3.6	80.7±5.3	85.1±3.5	89.5±8.6	89.5±4.3	91.3±4.4
	1.0	87.9±4.9	80.8±2.6	86.8±2.9	83.2±0.8	85.6±1.4	87.9±4.3
	10.0	81.6±0.4	80.7±0.4	82.5±2.5	83.3±1.3	82.3±1.9	80.9±0.6
Egg1	0.10	89.3±4.2	85.7±4.9	84.4±2.1	88.7±6.4	88.8±5.6	85.8±6.3
	0.50	86.1±5.4	90.3±2.1	83.0±1.8	87.6±7.4	85.5±4.7	90.4±4.7
	1.0	85.6±4.3	83.7±4.0	91.0±4.0	84.2±4.3	85.4±4.2	82.6±1.0
	10.0	86.4±0.9	82.4±1.5	82.6±1.9	82.9±1.2	85.4±2.3	86.7±1.5
Egg2	0.10	91.9±5.3	89.8±7.7	83.6±1.2	87.7±5.9	86.0±8.4	87.1±3.5
	0.50	84.6±3.0	89.1±5.5	88.8±7.3	83.9±3.3	88.2±2.9	84.9±1.9
	1.0	84.3±3.8	82.4±1.8	90.2±5.0	82.8±3.4	81.5±1.4	83.7±2.8
	10.0	89.7±0.7	88.5±1.0	88.2±2.1	88.4±1.4	86.5±1.7	82.5±0.9
Egg3	0.10	87.7±6.6	87.1±6.1	88.6±8.3	89.1±5.0	87.4±5.3	88.3±7.1
	0.50	85.8±3.4	85.0±6.4	87.2±8.4	83.8±4.9	90.5±2.7	84.4±1.6
	1.0	86.5±6.7	83.3±2.0	84.2±2.4	87.6±7.6	84.1±5.9	85.5±1.4
	10.0	80.8±0.5	84.4±0.9	88.4±2.2	83.1±2.6	85.5±2.0	82.0±1.7

Table S3 Comparison of the analytical performance of the developed MSPE sorbent with other methods

Analytical methods	Sample preparation method	Analytes	Sample amount	LOD (µg L^{-1}or µg kg^{-1})	Recovery (%)	RSD (%)	Reference
HPLC-UV	MIP-SPME	Ciprofloxacin, Norflorxacin	4 mL (Serum, plasma, tablet)	0.023-0.033	97-102	4.3–6.7	Mirzajani & Kardani, 2016
HPLC-UV	In-tube SPME	Ciprofloxacin, Enrofloxacin	15 mL (Water and urine)	0.01-0.05	92-106	5.4-11.1	Manbohi & Ahmadi, 2015
HPLC-DAD	MIP-SPE	Ciprofloxacin, Enrofloxacin, Norfloxacin	250 µL (Human urine)	39	42-96	4.7-8.0	de Oliveira et al., 2016
HPLC-DAD	MIP-SPE	Ciprofloxacin, Norfloxacin, Enrofloxacin	1 mL (Milk)	10-20	77-98	<8.3	G. N. Wang, Yang, Liu, Feng, & Wang, 2016
HPLC-DAD	DSPE	Ciprofloxacin, Difloxacin, Enrofloxacin, Sarafloxacin	2 g (Bovine milk, chicken muscle and egg)	0.05–0.3	97-99	3.4	X. He et al., 2017
HPLC-FLD and HPLC–MS	MIP-MISPE	Ciprofloxacin, Danofloxacin, Enrofloxacin, Norfloxacin, Sarafloxacin	10 mL(Chicken muscle)	0.2-2.7	68-102	<7	Urraca, Castellari, Barrios, & Moreno-Bondi, 2014
HPLC-FLD	SPE	Ciprofloxacin, Difloxacin, Enrofloxacin, Norfloxacin, Sarafloxacin	100 mL (Waste water)	0.3-1.5	79-96	<10.0	K. He & Blaney, 2015
HPLC-FLD	SBSE	Ciprofloxacin, Enrofloxacin, Norfloxacin	10 mL (chicken muscle and liver)	0.0045–0.0079	82-113	4.6-12.1	Fan, He, Wu, Chen, & Hu, 2015
HPLC-FLD	MSLM	Ciprofloxacin, Enrofloxacin, Norfloxacin,	6 mL (milk, eggs and honey)	0.07-0.53	92-105	0.65-5.28	Gao et al., 2015
HPLC-FLD	PANI/GOx/ C18-SiO_2-Fe_3O_4 alginate-MSPE	Ciprofloxacin, Danofloxacin, Difloxacin, Enrofloxacin, Norfloxacin, Sarafloxacin	10 mL (milk, honey, egg)	0.001-0.01	80-98	<9	This work

HPLC= High performance liquid chromatography; UV= Ultraviolet-Visible; DAD= Diode array detector; FLD= Fluorescence detector; MIP= Molecular imprinted polymer; SPME= Solid-phase microextraction; SPE= Solid phase extraction; SBSE= Stir bar sorptive extraction; MSLM= Magnetic-stirring salt-induced liquid–liquid microextraction; MSPE= magnetic solid phase extraction; PANI=Polyaniline; GOx=Graphene oxides

Paper III

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The enrichment and extraction of parabens with polydopamine-coated microporous carrageenan hydrogel beads incorporating a hierarchical composite of metal-organic frameworks and magnetite nanoparticles

Pattamaporn Klongklaew, Opas Bunkoed *

Center of Excellence for Innovation in Chemistry, Division of Physical Science, Faculty of Science, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

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ABSTRACT

A polydopamine-coated microporous composite of metal–organic frameworks and magnetite nanoparticles embedded in carrageenan hydrogel beads was fabricated and successfully utilized for the dispersive magnetic solid-phase extraction of parabens. Polydopamine and the metal organic frameworks enhanced the adsorption of parabens on the hierarchical composite sorbent by hydrogen bonding, hydrophobic and π-π interactions. The affecting parameters were optimized to achieve the highest extraction efficiency from rapid extraction with low solvent consumption. The developed method provided linearity from 0.10 to 100 μg L^{-1} of methyl parabens, 0.50–100 μg L^{-1} of ethyl paraben and 2.0–100 μg L^{-1} of propyl parabens and butyl paraben with low limit of detection (0.05–1.0 μg L^{-1}). When used to extract parabens in real samples, the composite adsorbent showed good accuracy, achieved extraction recoveries in the range of 80 to 96% and had a good stability which enabled reuse. The proposed hierarchical composite adsorbent could potentially be altered for the extraction of other compounds in various matrices.

1. Introduction

Parabens are preservatives that extend the life of products by controlling the growth of micro-bacteria. Owing to their broad spectrum antimicrobial properties, low toxicity and cost-effectiveness, they are extensively used in personal care products, cosmetics, toiletries, beverages and foodstuffs [1,2]. However, because of their stability and low volatility, parabens can accumulate in products and the environment. Exposure to parabens can disturb the human endocrine system, cause skin allergies and increase the risk of breast cancer [3,4]. To protect consumer health, the European Community (EC) has established the maximum allowed concentration of parabens in cosmetics at 8.0 g kg^{-1} [5]. Thus, the development of a simple, rapid and reliable method for the determination of parabens is necessary. Various methods have been reported for the analysis of parabens in different sample matrixes [6–10]. Among the reported methods, high performance liquid chromatography (HPLC) has been extensively used due to it can be used to simultaneously determine of many target analytes using separation column. However, parabens in real samples are normally present at trace level concentrations which cannot be directly detected among matric interferences. Consequently, sample preparation is a crucial step to preconcentrate the analyte and remove matric interferences [11–13].

Typical sample preparation methods used to extract parabens and remove interferences have included liquid–liquid extraction (LLE) [14], solid-phase extraction (SPE) [3,5] and solid phase microextraction (SPME) [15,16]. However, LLE method is time-consuming and uses large amounts of organic solvents. Also, SPE cartridges become plugged easily and some commercial sorbents are expensive [17]. The limitations of SPME include the insufficient chemical stability of the coating layer and high cost of the SPME fiber. The operational simplicity of the dispersive magnetic solid phase extraction (d-MSPE) technique has attracted much attention. Separation of the adsorbed analyte is accomplished by applying an external magnet and the method is compatible with various applications. The adsorbent used in d-MSPE can be fabricated from a variety of materials. Carrageenan hydrogel is an interesting supporting material which can entrap magnetite (Fe_3O_4) nanoparticles and affinity materials. It is nontoxic, biodegradable and easy to prepare [18]. To improve the extraction ability of the adsorbent toward analytes, various affinity materials have been incorporated or coated on the support. As well as carbon-based and polymer materials, metal organic frameworks (MOFs) have been used. MOFs are a class of hybrid organic–inorganic porous materials with large surface areas,

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* Corresponding author.
E-mail address: opas.b@psu.ac.th (O. Bunkoed).

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uniform structure cavities and good thermal stability [19]. One type of MOF which is an interesting material for the adsorption of parabens is MIL-101(Cr). This high affinity material is well suited to the extraction of target analytes since it has a cubic structure with a high surface area and good chemical stability [20,21]. Another interesting material is polydopamine (PDA) which can adsorb parabens via hydrogen bonding, π-π and hydrophobic interactions. These interactions can help to enhance adsorption.

In the present work, a composite mesoporous material was developed of Fe_3O_4 and MIL101, incorporated in carrageenan hydrogel beads coated with PDA. The developed material was used as a d-MSPE adsorbent for the enrichment and extraction of parabens. The developed hierarchical composite PDA@MIL101@Fe_3O_4@Car hydrogel bead was applied for the extraction of parabens in personal care products and its extraction efficiency was compared with the performance of a commercial solid phase extraction sorbent.

2. Experimental

2.1. Chemicals and reagents

Butyl 4-hydroxybenzoate (BP), ethyl 4-hydroxybenzoate (EP), methyl 4-hydroxybenzoate (MP), propyl 4-hydroxybenzoate (PP), terephthalic acid and k-carrageenan were purchased from Tokyo Chemical Industry Co. Ltd. (Japan). $FeCl_3·6H_2O$, $FeCl_2·4H_2O$, tris(hydroxymethyl) aminomethane and dopamine hydrochloride were from Sigma-Aldrich, (Germany). NH_4OH was from J.T.Baker (USA). Chromium (III) nitrate nonahydrate was purchased from HiMedia Laboratories Pvt. Ltd. (Nashik, India). Sodium acetate anhydrous was from Merck (Germany). Potassium chloride was from Ajax Finechem (New Zealand). Dimethylformamide, methanol, ethanol, acetonitrile and hydrochloric acid were from Labscan (Thailand).

2.2. Instrumental

The analysis of parabens was carried out using an Agilent 1100 HPLC system (Germany) coupled with a Fortis C18 reverse-phase column (5 μm, 4.6 × 150 mm I.D.) (Fortis Technologies Ltd., U.K). The diode array detector was used to detect parabens at 254 nm. The mobile phase consisted of water and acetonitrile (50:50 v/v) at a flow rate of 1.0 mL min^{-1}. The functional groups of the sorbent was investigated by Fourier transform infrared (FTIR) spectroscope (PerkinElmer, MA, USA). The surface morphology was examined by scanning electron microscope (JSM 5200 JEOL, Japan). A TriStar II 3020 surface area analyser (Micromeritics, USA) was used to investigate BET surface areas of composite sorbents. The bubbles inside the composite bead were observed by fluorescence stereomicroscope (M205FCA, Leica, Switzerland). Magnetic properties were investigated using a vibrating sample magnetometer (in-house), calibrated with a standard reference nickel sphere (model 730908). X-ray diffraction patterns were produced using the X′Pert-MPD (The Netherlands).

2.3. Preparation of the composite polydopamine-coated porous carrageenan/MIL101/magnetite nanoparticles adsorbent

The synthesis procedures of magnetite nanoparticles (Fe_3O_4) and MIL101 were modified from previous works [22,23]. For Fe_3O_4, 1.70 g of $FeCl_2·4H_2O$ and 4.70 g of $FeCl_3·6H_2O$ were prepared in deionized (DI) water (80 mL) and the mixture was transferred to a three-necked flask and heated at 80 °C under stirring at 800 rpm. Then, 10 mL of ammonium hydroxide was added into the mixture solution and heating continued for 1 h. The obtained Fe_3O_4 were collected by applying an external magnet. The collected Fe_3O_4 were washed with 100 mL of DI water and dried at 60 °C for 4 h. To synthesize MIL101, 2.0 g of Cr $(NO_3)_3·9H_2O$, 0.10 g of sodium acetate, 0.80 g of terephthalic acid and 25 mL of DI water were mixed and transferred to a Teflon-lined autoclave reactor and heated at 200 °C for 12 h. The green crystals produced were washed with 100 mL of DI water and once with 20 mL of dimethylformamide. The synthesized MIL101 was soaked in ethanol for 10 h to purify the product. Finally, the purified MIL101 was washed with DI water and dried at 80 °C for 24 h.

The preparation procedure of the hierarchical polydopamine-coated microporous MIL101@Fe_3O_4@Car hydrogel bead is illustrated in Fig. 1A. A carrageenan solution was prepared by dissolving 1.50 g of k-carrageenan in 100 mL of DI water and heating the solution at 50 °C for 1 h under stirring to obtain homogeneity. Then, 0.20 g of Fe_3O_4, 2.0 g of MIL101 and 0.50 g of $CaCO_3$ were mixed into the carrageenan solution. The homogeneous colloidal suspension was added dropwise into a 5.0% w/v KCl solution to create composite hydrogel beads, which were left immersed in the solution for 1 h to complete the formation of the hydrogel. The composite hydrogel beads were then soaked in HCl (20% w/v) for 3 min to produce a porous interior network which increased the surface area available to receive a polydopamine coating. After soaking in HCL solution, the hydrogel beads were washed with 100 mL of DI water until for three time. The washed composite MIL101@Fe_3O_4@Car hydrogel beads were incubated under stirring for 4 h in 100 mL of dopamine solution (10 mM) which was prepared in Tris-HCl buffer at pH 8.5. Finally, the fabricated hierarchical composite PDA@-MIL101@Fe_3O_4@Car hydrogel beads were separated from the dopamine solution, washed with DI water and kept in KCl solution until used.

2.4. Dispersive magnetic solid phase extraction procedure

The d-MSPE procedure using the composite PDA@-MIL101@Fe_3O_4@Car hydrogel beads is illustrated in Fig. 1B. Firstly, 0.75 g of PDA@MIL101@Fe_3O_4@Car beads were placed in a glass bottle containing 10.0 mL of standard or sample solution that was extracted for 10 min. The composite hydrogel beads with the adsorbed parabens were isolated using an external magnet and the remaining solution was poured off. The extracted parabens were desorbed from the composite adsorbent beads with 2.0 mL of a mixture of ethyl acetate and acetonitrile (50:50 v/v) under stirring for 15 min and the composite beads were separated from the desorption solution with a magnet. The desorption solution was evaporated at 50 °C and reconstituted with 1.0 mL of mobile phase before being injected into the HPLC-DAD system.

To obtain the highest extraction efficiency with short extraction time and low solvent consumption, the adsorbent preparation and extraction condition were studied. The type of sorbent, polymerization time, desorption condition, extraction time, adsorbent dosage, sample pH, ionic strength, stirring rate and sample volume were optimized. The efficiency of extraction was evaluated in terms of extraction recovery (ER), which was calculated as follows:

$$ER(\%) = (C_0V/C_xV_x) \times 100$$

where C_0 and C_x are the parabens concentration in reconstituted solvent (μg L^{-1}) and spiked sample, and V and V_x are the volume of the reconstituted solvent and spiked sample, respectively. The adsorption mechanism between parabens and the developed hierarchical composite hydrogel bead is shown in Fig. 1C.

3. Results and discussion

3.1. Characterizations of the hierarchical composite adsorbent

The fabricated hierarchical composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent was characterized using FTIR spectrophotometry, SEM technique, FSM microscope, VSM method, BET analysis and XRD spectroscopy. The FTIR technique was utilized to identify the functional groups of the developed adsorbent. The spectrum of carrageenan showed the bands of OH stretching and O-S-O symmetric vibration at 3432 and 1285 cm^{-1}, respectively (Fig. S1a). A strong peak of Fe-O-Fe was present at 586 cm^{-1} in the composite Fe_3O_4@Carrageenan

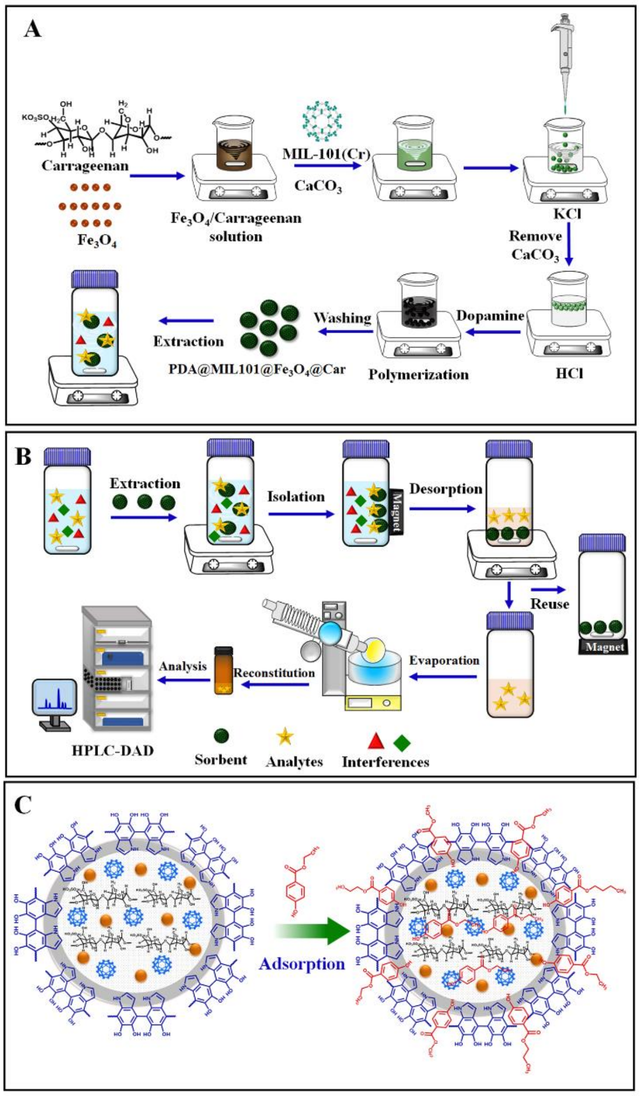

Fig. 1. The schemes show the fabrication procedure of PDA@MIL101@Fe_3O_4@Car hydrogel beads (A), the dispersive magnetic solid phase extraction procedure (B), and the interaction between parabens and the PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent (C).

spectrum (Fig. S1b). The MIL101@Fe_3O_4@Car spectrum showed peaks at 1618 and 1430 cm^{-1}, which due to C = C stretching of benzene and C-O-C stretching of dicarboxylate group in the MIL101 structure (Fig. S1c). The spectrum of the composite PDA@MIL101@Fe_3O_4@Car (Fig. S1d) showed the peaks of Fe-O-Fe stretching of Fe_3O_4, the O-S-O symmetric stretching and –OH stretching of carrageenan, the C = C and C-O-C stretching of MIL101 and NH_2 stretching of PDA. These results confirmed that Fe_3O_4, MIL101 and PDA were successfully incorporated with the carrageenan hydrogel bead.

The surface morphology of the composite adsorbent was investigated by SEM. In SEM images, carrageenan exhibited a smooth surface (Fig. 2A), while the MIL101 exhibited octahedral crystals (Fig. 2B). The

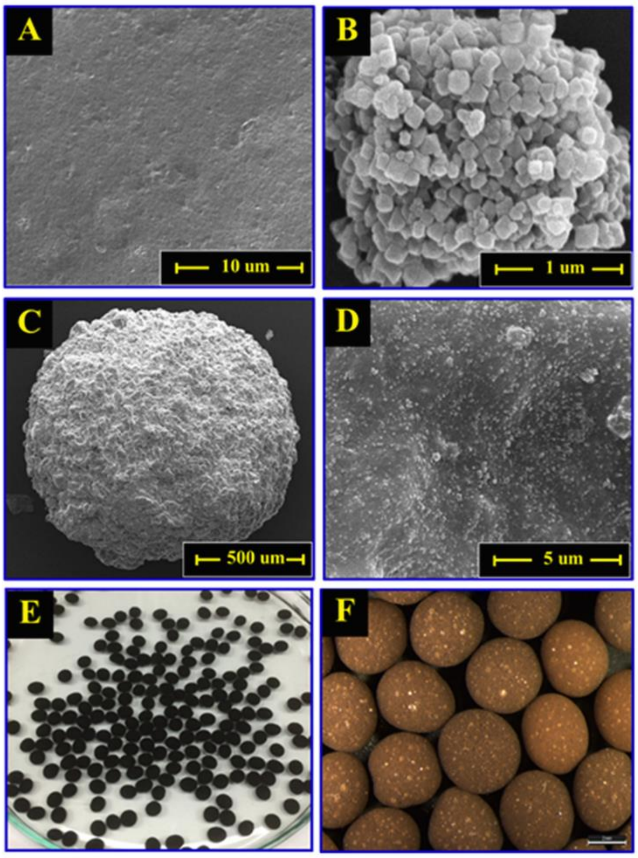

Fig. 2. SEM images show carrageenan (A), MIL101 (B), and a PDA@MIL101@Fe_3O_4@Car bead at 60X (C) and 10,000X (D). The photographs show the fabricated composite PDA@MIL101@Fe_3O_4@Car hydrogel beads in a petri dish (E) and the beads after soaking in HCl solution (F).

SEM images of the composite PDA@MIL101@Fe_3O_4@Car hydrogel (Fig. 2C and D) revealed the rough surface of the bead and PDA coating. Composite PDA@MIL101@Fe_3O_4@Car hydrogel beads were photographed unmagnified in a Petri dish (Fig. 2E). The image of hydrogel beads (Fig. 2F) was taken after the reaction of $CaCO_3$ and HCl which produced the hierarchical structure and CO_2 bubbles were visible inside the beads.

The magnetic properties of the composite PDA@MIL101@Fe_3O_4@Car hydrogel bead were studied using a VSM technique. The maximum saturation magnetization of the composite hydrogel beads was 3.428 emu g^{-1} (Fig. S2A). This result confirmed that magnetite nanoparticles were incorporated into the bead.

The surface areas of the composite Fe_3O_4@Car bead and the PDA@MIL101@Fe_3O_4@Car hydrogel bead were 0.9306 m^2 g^{-1} and 90.5823 m^2 g^{-1}, respectively. These results indicated that the integration of PDA and MIL101 with the hydrogel bead increased the surface area of the adsorbent to enhance the adsorption of the target analytes. The nitrogen adsorption–desorption isotherm of the composite PDA@MIL101@Fe_3O_4@Car hydrogel beads was a type IV and exhibited a hysteresis loop in the range of $0.8 < P/P_0 < 1.0$ (Fig. S2B).

The XRD pattern of the composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent showed the specific peaks of MIL101 and Fe_3O_4 (Fig. S2C). These results confirmed that both Fe_3O_4 and MIL101 were embedded in the hydrogel beads.

3.2. Optimization of composite adsorbent preparation and MSPE condition

3.2.1. Type of sorbent

To identify the most effective formulation of the adsorbent, parabens were extracted using the adsorbent at different stages of fabrication. The recoveries of composite hydrogel beads of Fe_3O_4@Car, MIL101@Fe_3O_4@Car, PDA@Fe_3O_4@Car and PDA@MIL101@Fe_3O_4@Car were 19–25%, 61–65%, 68–73% and 90–93%, respectively (Fig. S3). The composite PDA@MIL101@ Fe_3O_4@Car adsorbent provided the highest extraction recovery due to the integration of PDA and MIL101 which improved the adsorption of parabens on the composite adsorbent via π-π and hydrophobic interactions and hydrogen bonding. Therefore, the composite PDA@MIL101@ Fe_3O_4@Car hydrogel adsorbent was used for the extraction of parabens in further tests.

3.2.2. Polymerization time

The polymerization time of PDA was an important parameter for the fabrication of the composite adsorbent since it could affect the thickness of the polymer layer and, in turn, the interaction between PDA and parabens. The effect of PDA polymerization time was investigated at 2, 4 and 8 h (Fig. S4). The highest extraction recoveries were obtained with an adsorbent with a PDA coating polymerized for 4 h. Extraction recoveries decreased at a polymerization time of 2 h since the PDA was not completely self-polymerized. After the longer polymerization time of 8 h, recoveries also decreased since the PDA on the surface of sorbent was too thick, which reduced the surface area available for the adsorption of parabens. Thus, the fabrication of the composite PDA@ MIL101@-Fe_3O_4@Car hydrogel beads was completed by polymerizing PDA for 4 h.

3.2.3. Desorption conditions

The desorption solvent used could affect the elution of analytes from the composite adsorbent beads. Ethyl acetate, acetone, acetonitrile, methanol and a mixture of ethyl acetate and acetonitrile (1:1) were evaluated as desorption solvents. The highest recoveries were obtained using the mixture of ethyl acetate and acetonitrile (1:1) **(Fig. S5A)**. The volume of this desorption solvent was optimized from 1.0 to 4.0 mL. Recoveries of all four parabens were higher than 80% when using 2.0 mL of desorption solvent to elute analytes from the composite PDA@-MIL101@Fe_3O_4@Car adsorbent and rather constant when the volume of desorption solvent was more than 2.0 mL (Fig. S5B). Therefore, 2.0 mL of a mixture of ethyl acetate and acetonitrile (1:1) was used to desorb parabens from the composite PDA@MIL101@ Fe_3O_4@Car adsorbent in the remaining experiments.

3.2.4. Extraction times

The time required for the optimal adsorption of parabens on the composite PDA@MIL101@ Fe_3O_4@Car adsorbent was studied from 5 to 30 min. The parabens were completly adsorbed within 10 min (Fig. S5C) and 10 min was selected for the adsorption process in further experiments.

3.2.5. Amount of adsorbent

The lowest dose of adsorbent beads that obtained the highest extraction efficiency was investigated from 0.25 to 1.0 g. Extraction recoveries increased with increments of adsorbent dose from 0.25 to 0.75 g and then remained constant (Fig. S5D). Thus, 0.75 g was chosen for the extraction of parabens with the composite PDA@MIL101@ Fe_3O_4@Car hydrogel beads.

3.2.6. Sample pH and ionic strength

Sample pH can influence the interaction between an adsorbent and an analyte, and also affect the stability of the adsorbent. In this work, the pH of the parabens was adjusted incrementally from pH 4.0 to 8.0. The extraction recoveries of parabens were not significantly different, and all were higher than 80% (Fig. S6A). Sample pH did not affect the interaction between parabens and the composite adsorbent nor the stability of the composite adsorbent. Therefore, the adjustment of sample pH was not required. The ionic strength was also investigated for its effect on the solubility of parabens in the sample and the stability of the carrageenan hydrogel beads. Sodium chloride (NaCl) was applied at concentrations ranging from 0.0 to 10.0 %w/v (Fig. S6B). There was very little difference between the extraction efficiency obtained at 2.5% w/v NaCl and the extraction efficiency obtained without adjusting ionic strength. The addition of NaCl above 2.5 %w/v reduced extraction efficiency due to increased sample viscosity. Hence, the extraction of parabens with the composite PDA@MIL101@Fe_3O_4@Car adsorbent was performed without salt addition.

3.2.7. Stirring rate

The stirring rate applied to a sample solution can affect the partition between analytes and sorbent and here it was investigated from 500 to 1500 rpm. Increasing the stirring rate from 500 to 800 rpm increased extraction efficiency rapidly but increases from 800 to 1500 rpm consecutively reduced extraction efficiency (Fig. S6C). At low stirring rates, because the hydrogel bead adsorbents were not fully dispersed in the sample solution, mass transfer of analytes was too low but at high stirring speeds contact between analytes and adsorbent was too brief. Consequently, the stirring speed of 800 rpm was selected for d-MSPE of parabens sample solutions using the composite PDA@-MIL101@Fe_3O_4@Car adsorbent.

3.2.8. Sample volume

Sample volume is an important parameter of the sample preparation process because it affects both the extraction efficiency and enrichment factor. A large sample volume provides a high enrichment factor but it can cause an overload of adsorbent capacity. The sample volume in this study was evaluated from 5.0 to 20.0 mL. Good extraction efficiencies were obtained from sample volumes of 5.0 and 10.0 mL (Fig. S6D), however, 10.0 mL produced a higher enrichment factor. Therefore, a sample volume of 10.0 mL was used for the extraction of parabens using the composite PDA@MIL101@Fe_3O_4@Car adsorbent.

3.3. Adsorption studies

The adsorption kinetics were studied to determine the reaction mechanism driving the adsorption of parabens on the developed adsorbent. The pseudo-first-order, pseudo-second-order and intra-particle diffusion models were applied (Table S1). The amount of parabens adsorbed on the composite PDA@MIL101@Fe_3O_4@Car adsorbent was calculated from the following equation:

$$q_{e=}\frac{(C_0 - C_e)V}{m}$$

where q_e is the adsorption capacity (μg g^{-1}), C_0 and C_e are respectively the initial concentration of parabens and the concentration of parabens at equilibrium (μg L^{-1}), V is the volume of sample (L), and m is the amount of adsorbent (g). Of the three kinetic models (Fig. S7, S8 and S9), the correlation coefficient (R^2) of the pseudo-second-order was closest to unity, presenting the best fit. The result indicated that chemisorption was the mechanism by which parabens were adsorbed onto the developed composite adsorbent.

3.4. Analytical performance

The linearity, limit of detection (LOD) and limit of quantification (LOQ) were evaluated using the optimized conditions. The response of the composite PDA@MIL101@Fe_3O_4@Car hydrogel beads produced a good linearity from 0.10 to 100.0 μg L^{-1} of methyl paraben, from 0.50 to 100.0 μg L^{-1} of ethyl paraben and from 2.0 to 100.0 μg L^{-1} of propyl paraben and butyl paraben. R^2 were higher than 0.996 (Table 1). The LODs, based on a signal-to-noise ratio of 3, were 0.05 μg L^{-1} for methyl paraben, 0.15 μg L^{-1} for ethyl paraben, and 1.0 μg L^{-1} for propyl paraben and butyl paraben. The LOQs, based on a signal-to-noise ratio of 10, were 0.1 μg L^{-1} for methyl paraben, 0.5 μg L^{-1} for ethyl paraben, and 2.5 μg L^{-1} for propyl paraben and butyl paraben. These results indicated that the developed method was sufficiently sensitive to be utilized for the determination of trace parabens in real sample matrices.

3.5. Real sample analysis

The developed composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent was applied to extract and determine parabens in skin

Table 1

The performances of the composite PDA@MIL101@Fe_3O_4@Car hydrogel beads in the determination of parabens.

Analytes	Linear range (μg L^{-1})	Regression linear	R^2	LOD (μg L^{-1})	LOQ (μg L^{-1})
Methyl Paraben	0.1–100	y = (0.2009 ± 0.0034) x + (1.33 ± 0.14)	0.9979	0.05	0.1
Ethyl Paraben	0.5–100	y = (0.1894 ± 0.0041) x + (1.67 ± 0.17)	0.9972	0.15	0.5
Propyl Paraben	2.0–100	y = (0.1856 ± 0.0031) x + (1.37 ± 0.13)	0.9986	1.0	2.5
Butyl Paraben	2.0–100	y = (0.1906 ± 0.0041) x + (1.23 ± 0.16)	0.9968	1.0	2.5

cleansers and mouthwash. The analysis results are summarized in Table S2. Parabens were found in some samples but the found concentrations were lower than the maximum concentration allowed in cosmetics and personal care products. To evaluate the accuracy, the relative recovery was evaluated using standard solutions of parabens spiked in the samples at 5.0, 10.0 and 50.0 μg L^{-1}. The relative recovery was calculated based on the equation, Relative recovery (%) = (C_{Total}-C_{Sample})/C_{Spiked} *100, where C_{Total} is the total concentration of parabens found in the real sample after spiking with the standard, C_{Sample} is the original concentration of parabens in the real sample, and C_{Spiked} is the concentration of parabens spiked in the real sample. Relative recoveries from 80.4 to 95.6 with relative standard deviations < 7.1% were achieved (Table S3). The HPLC chromatograms of a real sample, a spiked sample and a standard solution of parabens are shown in Fig. 3. The good recoveries obtained implied that the developed composite PDA@MIL101@Fe_3O_4@Car hydrogel sorbent was efficient and could be used for the extraction of parabens in various matrix interferences before analysis by HPLC.

3.6. Reusability and reproducibility

The reusability of the composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent was evaluated after repeated extractions of parabens from spiked samples. After the first extraction cycle, the developed sorbent was washed with 2.0 mL of a 1:1 mixture of ethyl acetate and acetonitrile and 5.0 mL of 2.5 %w/v KCl. No carry-over effect was observed. The results showed that the extraction efficiency of the adsorbent did not significantly change for six extraction cycles (Fig. S10). Recovery decreased on the seventh cycle perhaps due to the loss of some of the PDA layer during the desorption step. The results implied that the developed composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent was sufficiently stable to allow reuse, reducing analysis cost and time spent in adsorbent preparation.

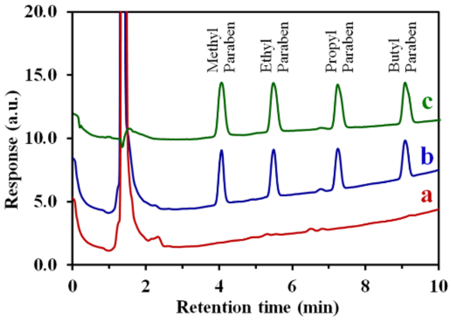

Fig. 3. HPLC chromatograms of a cleansing sample (a), a spiked cleansing sample (b) and a parabens standard (c).

The reproducibility of the composite PDA@MIL101@Fe_3O_4@Car hydrogel beads was examined by preparing six different lots in the same condition. The relative standard deviation of the recoveries of methyl paraben, ethyl paraben, propyl paraben and butyl paraben were 1.8, 2.6, 1.2 and 1.6%, respectively (Fig. S11), which are below the acceptable value for an AOAC standard method of<16%. The results demonstrated that the preparation process of the developed composite adsorbent had a good reproducibility.

3.7. Comparison with solid phase extraction sorbent and other methods

The extraction efficiency of the developed composite PDA@MIL101@Fe_3O_4@Car adsorbent was compared with a commercial solid phase extraction sorbent (SPE-Oasis HLB sorbent). The recovery of the developed adsorbent was not significantly different than the extraction efficiency of the SPE-C18 sorbent (Fig. S12). The results supported the use of the composite PDA@MIL101@Fe_3O_4@Car hydrogel for the extraction of parabens in real samples with different matrix interferences.

The performance of the developed d-MSPE method using the composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent was compared with the performances of reported methods used for the extraction of parabens in a variety of samples (Table 2). The analytical performances of the developed method, including LOD, recovery, and relative standard deviation, were better or comparable with the reported methods. However, the developed composite adsorbent is eco-friendly, comprising substances of low toxicity and good biodegradability, and reusable (6 cycles). In addition, d-MSPE adsorbent can easily separate from sample solution without the filtration or centrifugation steps normally required in other sample preparation methods. The comparison of analytical performances indicated that the composite PDA@MIL101@Fe_3O_4@Car beads were suitable for quantitative analysis of parabens in highly complex matrices.

MNP@DC193C = Magnetic nanoparticles functionalized water soluble surfactant type DC193C; MSPE = Magnetic solid phase extraction; MNP-PTMS@CTF = Magnetic nanoparticles modified with phenyltrimethoxysilane functionalized with covalent triazine-based frameworks; PPY-Ag NPs = Polypyrrole-silver nanoparticles; HF = Hollow fiber; VMDB = 1-vinylbenzyl-3-methylimidazolium hexafluorophosphate and divinylbenzene copolymer; PIL = Polymeric ionic liquid; prGO/Mg-Al LDH = Magnesium-aluminum layered double hydroxide functionalized with partially reduced graphene oxide; μSPE = Micro solid phase extraction; CUR-MGO = Curcumin loaded magnetic graphene oxide; MIP-OT = Molecularly imprinted polymer layer open tubular; PA/GO/PPy = Polyamide-graphene oxide-polypyrrole; SC-μSPE = Spin column micro SPE; SWNH = Single-walled carbon nanohorn; ME-MB/IT = magnetism-enhanced monolith-based in-tube.

4. Conclusion

A composite adsorbent was fabricated of MIL101 and magnetic nanoparticles embedded in carrageenan hydrogel beads that were then coated with polydopamine. The adsorbent beads were successfully developed for the extraction and enrichment of parabens. The magnetic nanoparticles enabled the rapid separation of the sorbent from the sample solution to reduce extraction time. MIL101 and polydopamine can adsorb parabens via π-π, hydrophobic interaction and hydrogen bonding, which improved extraction efficiency. In addition, the composite hydrogel beads were simple to fabricate in mild conditions and the carrageenan supporting material is of low toxicity. The composite PDA@MIL101@Fe_3O_4@Car hydrogel sorbent exhibited good extraction efficiency, reproducibility and reusability. The developed composite dispersive magnetic solid-phase extraction adsorbent is environmentally friendly, convenient to use, easy to prepare and can be applied for the

Table 2
A comparison of the performance of the developed d-MSPE sorbent with the performances of methods previously used for the determination of parabens.

Analytical method	Sample preparation method	Parabens	Sample amount	LOD(μg L^{-1}or μg kg^{-1})	Recovery (%)	RSD(%)	Reference
HPLC-UV	MNP@DC193C/MSPE	MP, EP, PP, BP	80 mL(Water)	2.4–6.3	86–118	0.41–15.9	[17]
HPLC-UV	MNP-PTMS@CTF/MSPE	MP, EP, PP, BP	7 mL(Milk, Urine, Sunscreen cream, Herbal hair tonic, Shower wastewater)	0.02	86–102	2.3–5.0	[24]
HPLC-UV	PPY-Ag NPs/HF-SPME	MP, EP, PP	30 mL(Water, Fruit juice, and Beer)	0.01	90–104	2.4–3.1	[2]
HPLC-DAD	VMDB/PIL-MA-MSPE	MP, EP, PP, BP	-(Water, Fruit juice)	0.05–0.17	83–108	2.1–7.8	[25]
HPLC-UV	prGO/Mg-Al LDH/ μSPE	MP, EP, PP	-(Milk)	3.0–5.0	87–104	4.3–8.9	[26]
HPLC-DAD	CUR-MGO /DMSPE	MP, EP, PP, BP	20 mL (Toothpaste and Mouthwash)	0.4–1.0	71–120	1.9–7.7	[5]
HPLC-UV	Coiled MIP-OT capillary tube	MP, EP, PP, BP	30 mL(Personal care and Cosmetic products)	0.2–0.3	91–105	2.1–4.3	[27]
HPLC-UV	PA/GO/PPy /SC-μSPE	MP, EP, PP	5 mL(Milk)	3.0–7.0	81–97	2.7–8.6	[28]
HPLC-UV	SWNH-monolithic tip	MP, EP, PP, BP	2 mL(Urine)	1.0–7.0	80–116	1.0–13.0	[29]
HPLC-DAD	Online ME-MB/IT-SPME	PP, BP	1.2 mL(Water and Grape juice)	0.01–0.05	86–114	0.9–7.7	[30]
HPLC-DAD	PDA@MIL101@Fe_3O_4@Car d-MSPE	MP, EP, PP, BP	10 mL(Skin cleanser and mouthwash)	0.05–1.0	80–96	1.0–7.1	This work

extraction of parabens in various matrix interferences.

CRediT authorship contribution statement

Pattamaporn Klongklaew: Methodology, Software, Validation, Visualization, Writing - original draft. **Opas Bunkoed:** Conceptualization, Formal analysis, Investigation, Resources, Data curation, Supervision, Project administration, Funding acquisition, Writing - review & editing.

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.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.microc.2021.106103.

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Supplementary material

The enrichment and extraction of parabens with polydopamine-coated microporous carrageenan hydrogel beads incorporating a hierarchical composite of metal-organic frameworks and magnetite nanoparticles

Pattamaporn Klongklaew, Opas Bunkoed*

Center of Excellence for Innovation in Chemistry, Division of Physical Science, Faculty of Science, Prince of Songkla University, Hat Yai, Songkhla 90112, Thailand

Corresponding author**:** Opas Bunkoed, Ph.D.

Email address**:** opas.b@psu.ac.th

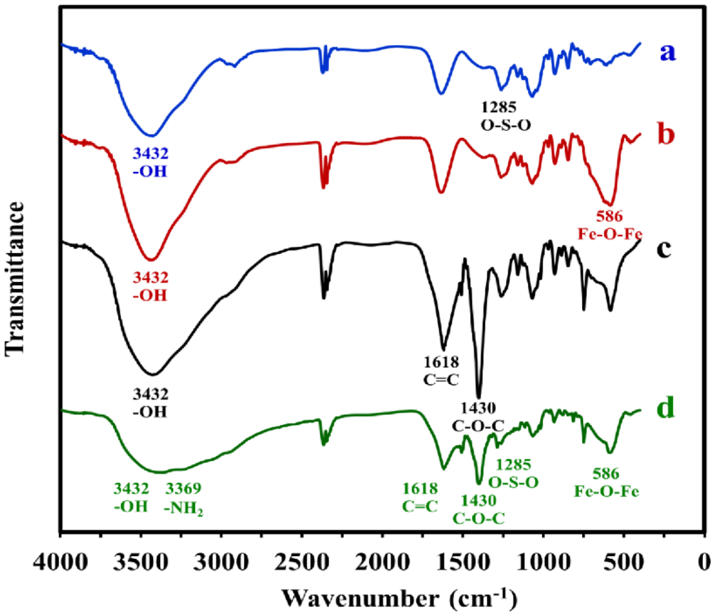

Fig. S1 FTIR spectra of carrageenan (a), Fe$_3$O$_4$@Car (b), MIL101@Fe$_3$O$_4$@Car (c) and PDA@MIL101@Fe$_3$O$_4$@Car (d)

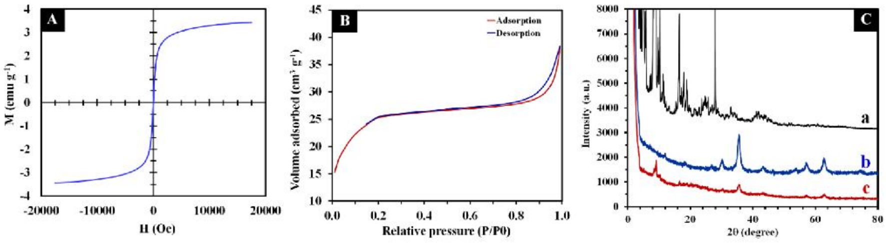

Fig. S2 VSM curve of the nanocomposite hydrogel bead (A), the nitrogen adsorption and desorption isotherms of the composite Fe_3O_4@Car hydrogel (B) and the XRD diffraction patterns (C) of MIL101 (a), Fe_3O_4 nanoparticle (b), composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent (c)

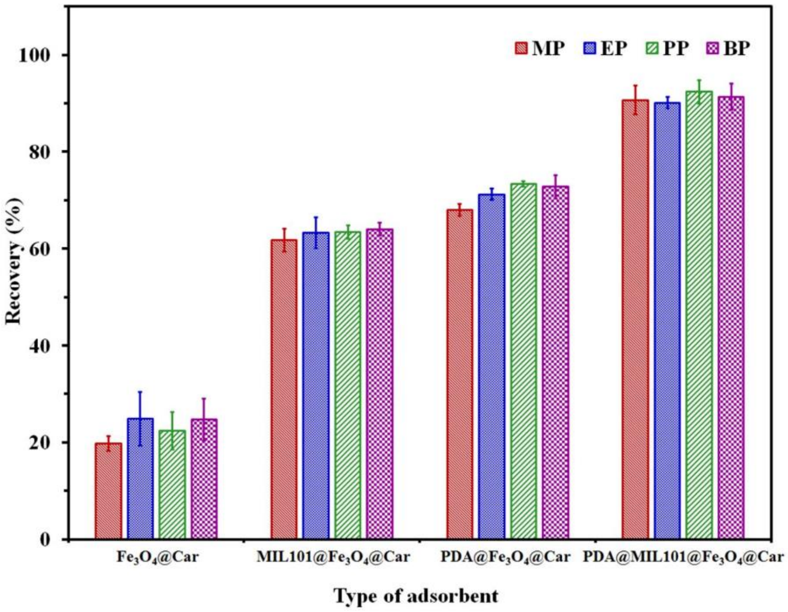

Fig. S3 The chart shows recoveries of parabens by different formulations of the composite adsorbent.

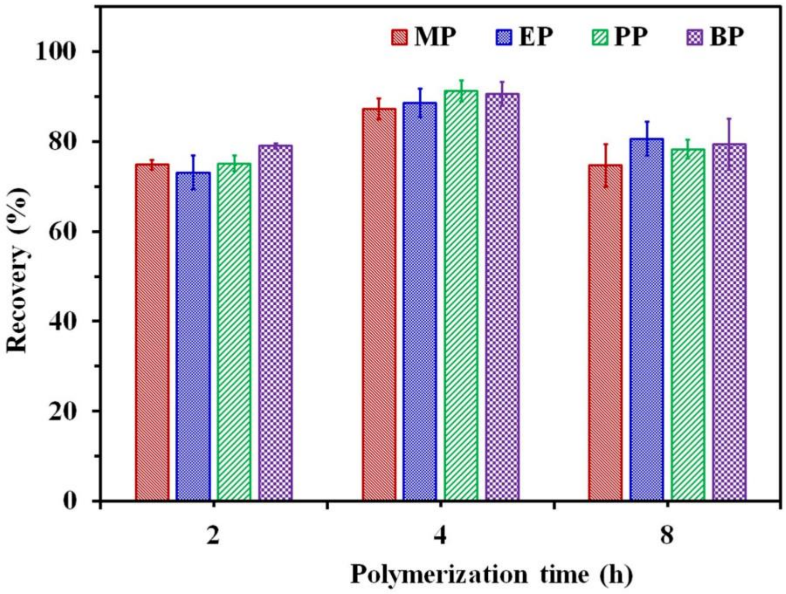

Fig. S4 The chart shows the effect of polymerization time of polydopamine on the extraction of parabens using the composite PDA@ MIL101@Fe_3O_4@Car hydrogel beads.

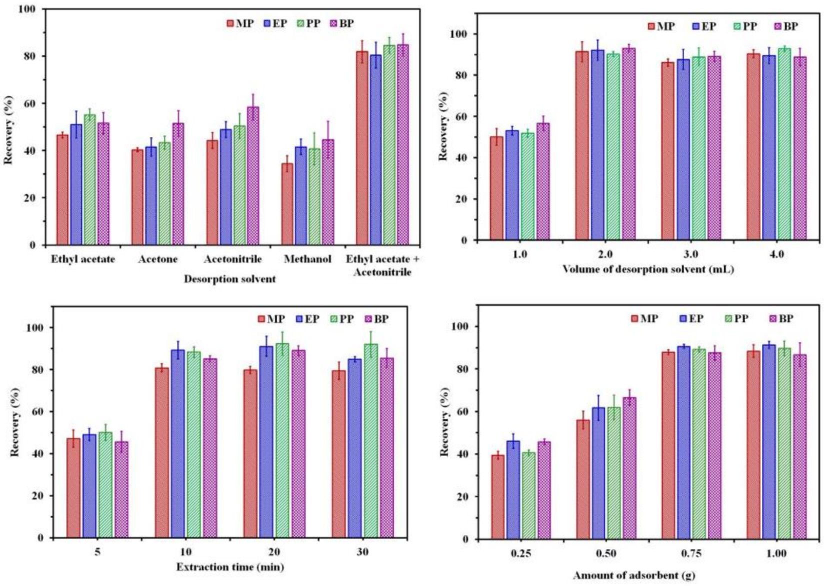

Fig. S5 The charts illustrate the effects on the extraction of parabens of different desorption solvents (A), desorption solvent volume (B), extraction time (C) and adsorbent dosage (D).

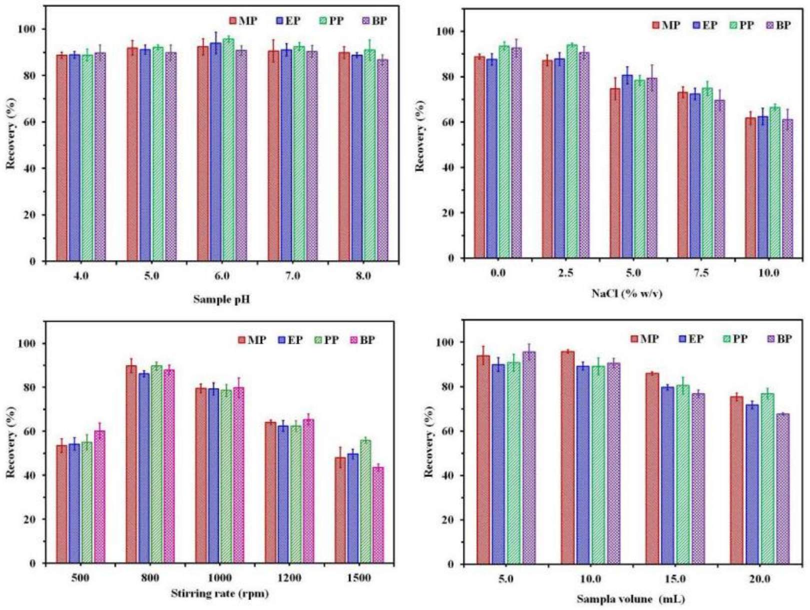

Fig. S6 The charts show the effects on the extraction of parabens of sample pH (A), ionic strength (B), stirring rate (C) and sample volume (D) using the composite PDA@MIL101@Fe_3O_4@Car adsorbent beads.

Table S1. The kinetic equation and linear plots of the three applied kinetic models

Kinetic model	Equation	Linear plot
Pseudo-first-order	$\mathrm{In}(q_e - q_t) = \mathrm{In}q_e - k_1t$	$\mathrm{In}(q_e - q_t)$ Vs. t
Pseudo-second-order	$\frac{t}{q_t} = \frac{1}{k_2{q^2}_e} + \frac{t}{q_e}$	$\frac{t}{Q_t}$ Vs. t
Intraparticle diffusion	$q_t = k_3t^{1/2} + c$	q_t Vs. $t_{1/2}$

q_t (µg g^{-1}) = the adsorption capacity at time t; k_1, k_2 and k_3 (min^{-1}) are the rate constants of the pseudo-first-order, pseudo-second-order and intraparticle diffusion models, respectively; and c is the intercept.

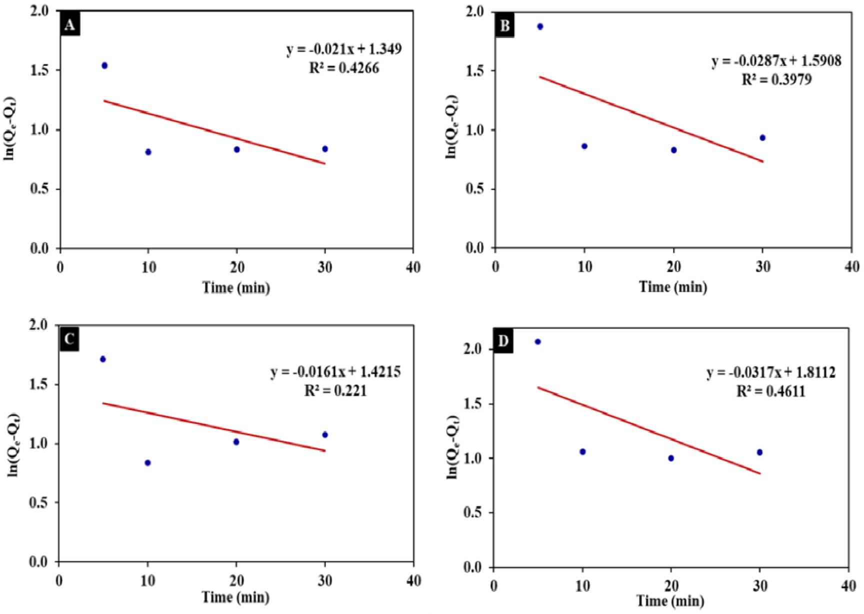

Fig. S7 The plots were produced by applying the pseudo-first-order kinetic model to the adsorption of methyl paraben (A), ethyl paraben (B), propyl paraben (C) and butyl paraben (D) on the composite PDA@MIL101@ Fe_3O_4@Car hydrogel adsorbent.

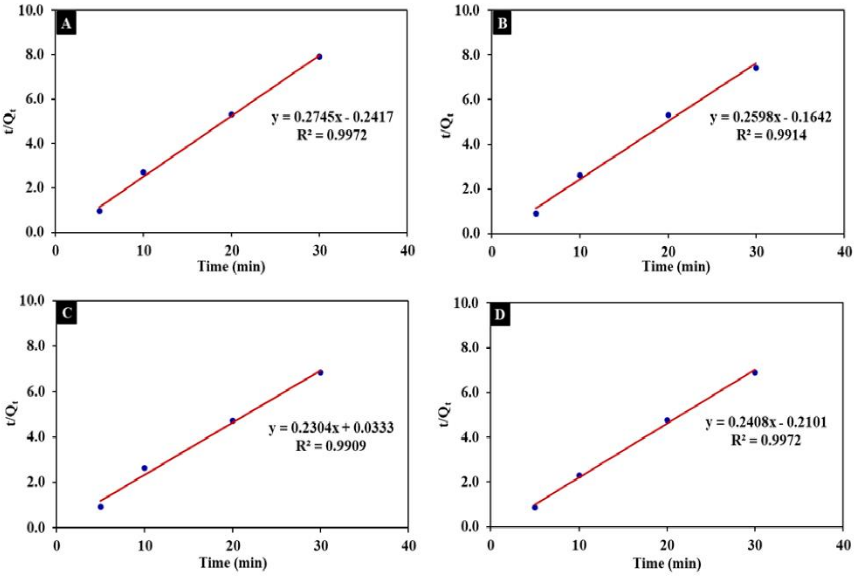

Fig. S8 The plots were produced by applying the pseudo-second-order kinetic model to the adsorption of methyl paraben (A), ethyl paraben (B), propyl paraben (C) and butyl paraben (D) on the composite PDA@MIL101@ Fe_3O_4@Car hydrogel adsorbent.

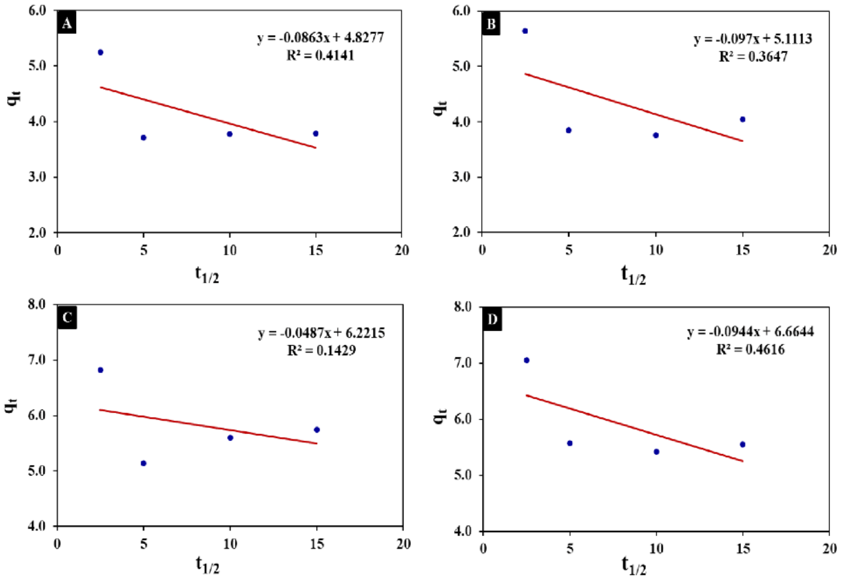

Fig. S9 The plots were produced by applying the intraparticle diffusion model to the adsorption of methyl paraben (A), ethyl paraben (B), propyl paraben (C) and butyl paraben (D) on the composite PDA@MIL101@ Fe_3O_4@Car hydrogel adsorbent

Table S2. The determination of parabens in real samples using composite PDA@MIL101@Fe_3O_4@Car hydrogel beads coupled with HPLC-DAD

Samples	Concentration (μg mL^{-1})			
	Ethyl Paraben	Methyl Paraben	Propyl Paraben	Butyl Paraben
Skin cleanser 1	ND	<LOQ	ND	0.010±0.002
Skin cleanser 2	0.051±0.020	ND	ND	ND
Skin cleanser 3	ND	ND	ND	ND
Mouthwash 1	24.628±0.044	0.018±0.002	6.579±0.059	0.010±0.008
Mouthwash 2	0.038±0.009	ND	<LOQ	0.026±0.017
Mouthwash 3	<LOQ	0.022±0.001	ND	<LOQ

ND=not detectable

Table S3. The extraction recoveries of parabens in spiked samples using composite PDA@MIL101@Fe_3O_4@Car hydrogel beads coupled with HPLC-DAD

Samples	Added (μg L^{-1})	Recovery (%)			
		Ethyl paraben	Methyl paraben	Propyl paraben	Butyl paraben
Skin cleanser 1	5	91.8±5.6	92.9±5.3	86.5±5.3	85.9±4.1
	10	87.4±1.9	86.8±1.6	86.5±3.4	84.5±5.4
	50	82.2±1.4	83.3±1.8	88.7±1.4	81.4±1.8
Skin cleanser 2	5	90.4±4.3	85.8±7.1	84.4±6.0	87.2±6.7
	10	85.1±6.1	84.9±5.4	84.3±4.9	82.7±4.3
	50	82.1±2.0	88.3±2.3	86.2±1.8	83.0±2.0
Skin cleanser 3	5	86.9±5.5	85.5±6.0	81.8±5.8	86.1±5.4
	10	84.7±1.9	83.8±1.8	87.1±4.9	83.9±3.6
	50	81.5±1.0	86.2±2.0	85.4±1.4	84.7±2.0
Mouthwash 1	5	85.2±6.0	84.9±6.0	83.0±3.5	81.2±1.5
	10	91.2±3.3	88.0±6.6	86.6±2.6	82.9±5.3
	50	82.6±2.0	93.1±1.5	88.0±4.6	90.5±1.1
Mouthwash 2	5	80.4±4.9	86.8±2.3	83.4±3.0	85.4±5.1
	10	85.4±6.4	85.4±4.8	82.0±1.6	80.9±1.7
	50	95.6±2.3	91.5±2.8	91.4±2.4	92.9±1.5
Mouthwash 3	5	80.8±5.4	83.1±3.8	83.6±6.4	85.5±5.5
	10	86.7±3.7	89.2±3.2	81.5±4.9	91.9±1.1
	50	86.9±1.3	89.3±2.1	92.1±1.4	91.3±3.6

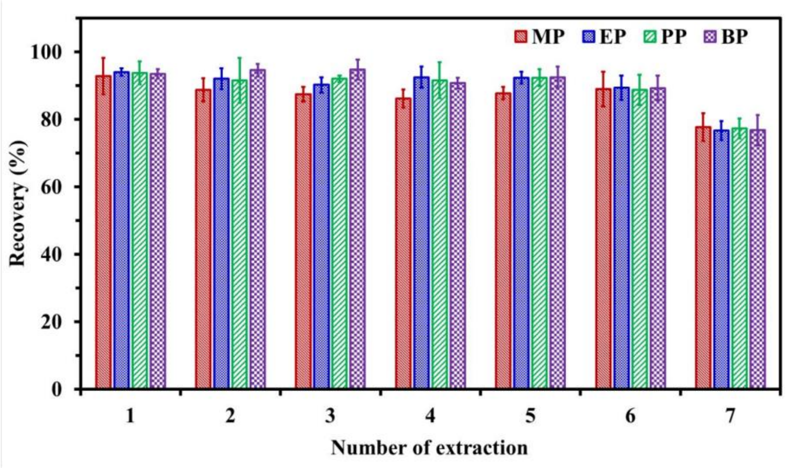

Fig. S10 The chart shows the reusability of the composite PDA@MIL101@Fe_3O_4@Car hydrogel bead for the extraction of parabens.

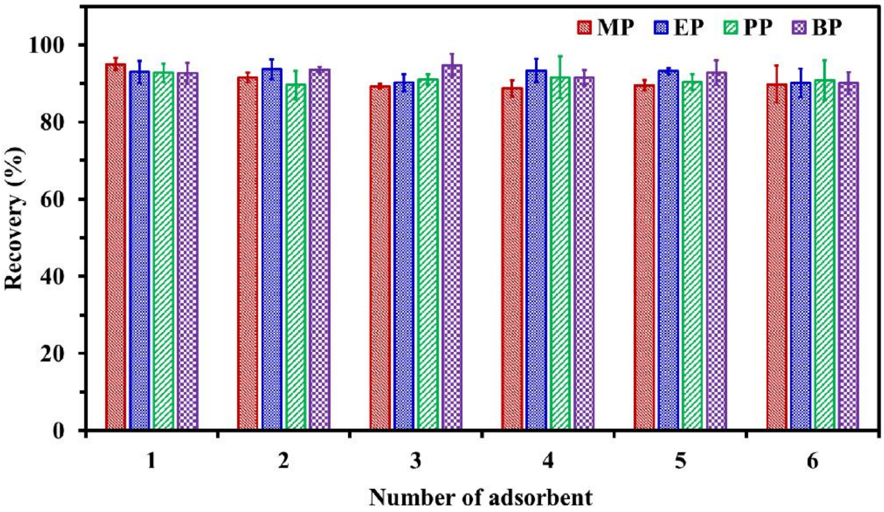

Fig. S11 The reproducibility of the developed composite PDA@MIL101@Fe_3O_4@Car hydrogel bead for the extraction of parabens

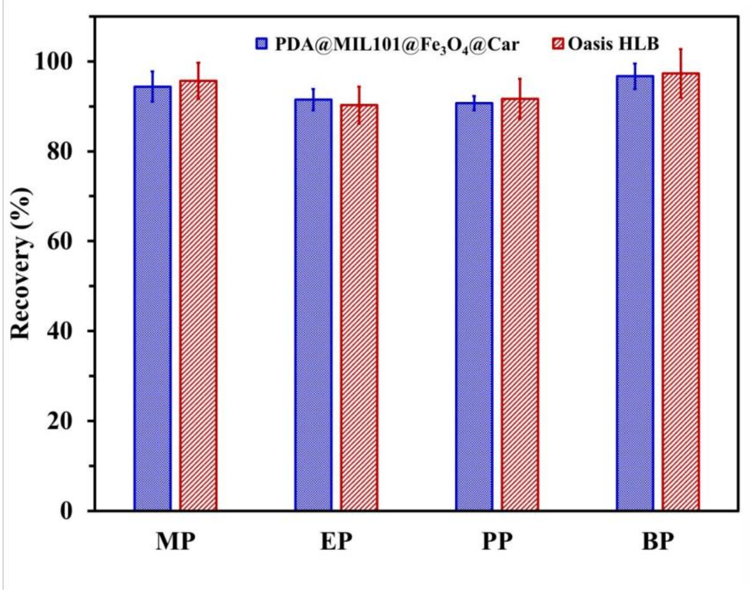

Fig. S12 The recoveries of parabens using the composite PDA@MIL101@Fe_3O_4@Car hydrogel adsorbent and the SPE-Oasis HLB sorbent

VITAE

Name Miss Pattamaporn Klongklaew

Student ID 6010230013

Education Attainment

Degree	Name of Institute	Year of Graduation
Bachelor of Science (Chemistry)	Prince of Songkha University	2017

Scholarship Award during Enrolment

The National Research Council of Thailand (NRCT), Thailand Science Research and Innovation (TSRI), The Royal Golden Jubilee PhD (RGJ), Center of Excellence for Innovation in Chemistry (PERCH-CIC), Division of Physical Science, Faculty of Science, Prince of Songkla University

List of Publication

Klongklaew, P., Naksena, T., Kanatharana, P., Bunkoed, O., A hierarchically porous composite monolith polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and pre-concentration of carbamate pesticides in fruit juices. ***Analytical and Bioanalytical Chemistry*** 410(27) (2018), 7185-7193.

Klongklaew, P., Kanatharana, P., Bunkoed, O., Development of doubly porous composite adsorbent for the extraction of fluoroquinolones from food samples. ***Food Chemistry*** 309 (2020), 125685.

Klongklaew, P., Bunkoed, O., The enrichment and extraction of parabens with polydopamine-coated microporous carrageenan hydrogel beads incorporating a hierarchical composite of metal-organic frameworks and magnetite nanoparticles. ***Microchemical Journal*** 165 (2021), 106103.

Orachorn, N., **Klongklaew, P.**, Bunkoed, O., A composite of magnetic GOx@MOF incorporated in alginate hydrogel fiber adsorbent for the extraction of phthalate esters. ***Microchemical Journal*** 171 (2021), 106827.

Oral Presentation

Klongklaew, P., Kanatharana, P., Bunkoed, O., A porous monolith composite cryogel sorbent for the extraction and determination of carbamate pesticides in fruit juices, TSRI CONGRESS 2019 “Disruptive Technology for World Society”, 8-9 August 2019, Pathumwan Princess Hotel, Bangkok, Thailand.

Klongklaew, P., Kanatharana, P., Bunkoed, O., A porous monolith composite cryogel sorbent for the extraction and determination of carbamate pesticides in fruit juices, RGJ-University Forum (Southern region), 27 May 2019, Prince of Songkha University, Songkhla, Thailand.

Poster Presentation

Klongklaew, P., Kanatharana, P., Bunkoed, O., A composite octadecyl/graphene oxide/chitosan cryogel sorbent for extraction and determination of pesticides in fruit juices, Pure and Applied Chemistry International Conference 2018, 7-9 February 2018, Prince of Songkha University, Songkhla, Thailand.

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Klongklaew, P., Kanatharana, P., Bunkoed, O., A porous monolith composite polypyrrole/octadecyl silica/graphene oxide/chitosan cryogel sorbent for the extraction and enrichment of carbamate pesticides in fruit juices, the 6th NRCT-IFS-PERCH-CIC Workshops: ASEAN Research and

Innovation Initiatives, 19-24 February 2019, Chiang Mai Grandview Hotel & Convention Center, Chiang Mai, Thailand.

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Klongklaew, P., Kanatharana, P., Bunkoed, O., A doubly porous microcomposite magnetic sorbent for the extraction and determination of fluoroquinolones in food samples, Pure and Applied Chemistry International Conference 2020, 13-14 February 2020, IMPACT Forum, Mauangthong Thani, Bangkok, Thailand.

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