ANALYTICAL METHODOLOGY BASED ON A SILICONE ROD (SR) MICROEXTRACTION COMBINED WITH HPLC-DAD METHOD FOR THE DETERMINATION OF PHARMACEUTICALS AND ANTIBACTERIAL PRODUCTS IN EFFLUENT WASTEWATERS. CHARACTERIZATION OF THE SORPTION REMOVAL PROCESSES BY CORK

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Université de Sfax

DOCTORAL THESIS

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Doctoral program in chemistry

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Presented in partial fulfilment of the requirements for a doctoral degree from the University of Girona

Dr. Victòria Salvadó Martín of University of Girona and Dr. Abdelhamid Ben Salah of University of Sfax

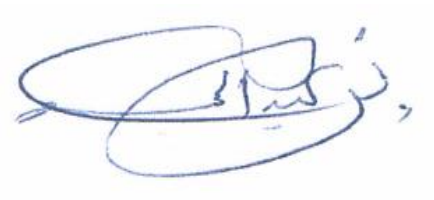
WE DECLARE:

That the thesis entitled: "***Analytical methodology based on a silicone rod (SR) micro-extraction combined with HPLC-DAD method for the determination of pharmaceuticals and antibacterial products in effluent wastewaters. Characterization of the sorption removal processes by cork****",* presented by **Maryam Mallek** to obtain a doctoral degree, has been completed under our supervision**.**

For all intents and purposes, we hereby sign this document.

Dr. Victòria Salvadó Martín

Dr. Abdelhamid Ben Salah



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In the end, I would like to extend my thanks to everyone who has helped me directly or indirectly with this doctoral thesis. I dedicate it to them.

Maryam

LIST OF ABREVIATIONS

AC	Activated carbon
ACN	Acetonitril
APCI	Atmospheric pressure chemical ionisation
AOP	Advanced oxidation processes
BSTFA	Bis(trimethylsilyl)trifluoroacetamide
BAμE	Bar adsorptive microextraction
BPA	Bisphenol A
CBZ	Carbamazepine
CPs	Chlorophenols
CE	Capillary electrophoresis
CA	Clofibric acid
CME	Capillary microextraction
CAR	Carboxen
CWX	Carbowax
CNPrTEOS	Cyanopropyltriethoxysilane
CNTs	Carbon nanotubes
CI	Chemical ionization
2-CP	2-Chlorophenol
CAS	Conventional activated sludge
DEET	N,N-diéthyl-3-methylbenzamide
DCF	Diclofenac
Diclofenac-Na	Diclofenac sodium salt
DFPSE	Dynamic fabric phase sorptive extraction
DI	Direct immersion
DVB	PDMS/divinylbenzene
2,4-DCP	2,4-dichlorophenol
EF	Enrichment factor

EPA	Environmental Protection Agency
EDCs	Endocrine disruptor compounds
EDMA	Ethylene glycol dimethacrylate
EU	European Union
EG	Ethylene glycol
ECD	Electron capture detector
ESI	Electrospray ionisation
EI	Electron impact
FID	Flame ionization
FL	Fluorescence
FPSE	Fabric phase sorptive extraction
GC	Gas chromatography
GC-MS/MS	Gas chromatography-tandem mass spectrometry
GC-FID	Gas Chromatography-Flame Ionization Detector
GAC	Granular activated carbon
GO	Graphen oxides
HPLC	High performance liquid chromatography
HPLC-DAD	High performance liquid chromatography with a diode array detector
HPLC UV-vis	Liquid chromatography with ultraviolet-visible detection
HILIC	Hydrophilic interaction liquid chromatography
HF-LPME	Hollow-fibre liquid-phase microextraction
HEMA	2-hydroxyethyl methacrylates
HS	Headspace
IBP	Ibuprofen
ILC	Isotope-labelled compounds
IP-LC	Ion-pair liquid chromatography
Kow	Octanol water partition coefficient
Kv	Kevlar
KTP	Ketoprofen

LOD	Limit of detection
LOQ	Limit of quantification
LC	Liquid chromatography
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LC-ESI-MS/MS	Liquid chromatography- electrospray ionisation- tandem mass spectrometry
LD	Liquid desorption
LPME	Liquid phase microextraction
LLE	Liquid-liquid extraction
MESCO	Membrane-enclosed silicone collector
MIPs	Molecularly imprinted polymers
MPB	Methyl paraben
MS	Mass spectrometry
MTBSTFA	N-tertbutyldimethylsilyl-N-methyltrifluoroacetamide
MeOH	Methanol
MSAμE	Multi sphere adsorptive microextraction
4-MBC	4-methyl-benzylidene-camphor
NAP	Naproxen
NPs	Nitrophenols
2-NP	2-Nitrophenol
NSAIDs	Non-steroidal anti-inflammatory drugs
NVP	N-vinylpyrrolidone polymer
NPD	Nitrogen-phosphorus detector
NPLC	Normal phase liquid chromatography
Ops	Organophosphates
PPCPs	Pharmaceutical and personal care products
PEGMA	Polyethylene glycol monoethylacrylate
PETRA	Pentraerythritoltriacrylate
PES	Polyethersulfone
PP	Polypropylene

PCP	Personal care products
Ph	Phenol
PCP	Pentachlorphenol
PA	Polyacrylate
PEG	Polyethylene glycol
PAC	Powdered activated carbon
PDMS	Polydimethylsiloxane
RDSE	Rotating disk sorptive extraction
RSD	Relative standard deviation
RBA	Rice bran ash
RPLC	Reversed phase liquid chromatography
SPE	Solid-phase extraction
SPME	Solid-phase microextraction
SBSE	Stir bar sorptive extraction
SRSE	Stir-rod-sorptive extraction
SDME	Single drop microextraction
SCSE	Stir-cake-sorptive extraction
SR	Silicone rod
ST	Silicone tube
SEM	Scanning electron microscopy
TFME	Thin-film microextraction
TD	Thermal desorption
TCS	Triclosan
TCD	Thermal conductivity detector
VP	Vinylpyridine
WWTPs	Wastewater treatment plants

INDEX OF FIGURES

INDEX OF TABLES

Contents

Resum

El control de la contaminació causada tant per microcontaminants orgànics regulats i no regulats és de gran importància ja que derivats fenòlics, productes farmacèutics i d'higiene personal s'han detectat, a nivells de concentració traça, en els efluents d'entrada i sortida de les depuradores d'aigües residuals. En el grup de fàrmacs detectats, hi ha antiinflamatoris no esteroïdals com el ketoprofén (KTP) i el naproxén (NAP), antiepilèptics, com la carbamazepina (CBZ) i analgèsics, com el diclofenac sòdic (DCF), i entre els productes d'higiene personal, antisèptics com ara el triclosan (TCS) i conservants, com el metil paraben (MPB), tots aquests compostos es consideren contaminants emergents, ja que potencialment poden afectar als ecosistemes aquàtics i la salut humana. Encara que la majoria d'aquests compostos no estan regulats, el diclofenac s'ha inclòs en la llista de contaminants prioritaris de la UE i el TCS ha estat classificat com a contaminant d'alta prioritat per l'Agència de Protecció Ambiental (EPA) dels Estats Units (USA). Els fenols, que són disruptors endocrins, també estan a la llista de contaminants prioritaris de l'EPA. Tenint en compte que les plantes de tractament d'aigües residuals i industrials, no estan dissenyades per eliminar microcontaminants orgànics i que a més, molts d'aquests compostos són poc biodegradables, els efluents d'aigües residuals tractades que els contenen són una de la fonts principals d'introducció d'aquests contaminants en rius i llacs que són reservoris d'aigua potable. Per tant, cal controlar la presència de microcontaminants orgànics en les masses d'aigua atès els seus possibles impactes ambientals associats al seu gran ús, freqüència de detecció i persistència. S'han proposat moltes metodologies analítiques per a determinar les diferents famílies de microcontaminants orgànics, inclosos els fàrmacs i ingredients de productes d'higiene personal (PPCPs), la majoria d'aquests mètodes es basen en l'anàlisi de les aigües per cromatografia líquida amb detecció espectrofotomètrica (Uv-vis) o per espectrometria de masses (MS). Les baixes concentracions, $ng.L^{-1}$ o pocs $mg.L^{-1}$, dels microcontaminants orgànics esmentats en les aigües superficials requereixde l'aplicació d'etapes d'enriquiment i purificació de les mostres abans de la seva anàlisi cromatogràfica, fins i tot, en el cas que s'utilitzi la detecció per MS. S'han desenvolupat diverses tècniques d'extracció i preconcentració per a l'extracció d'analits a partir de mostres aquoses. Les tècniques convencionals de preparació de mostres són l'extracció de líquid-líquid (LLE) i l'extracció en fase sòlida (SPE) que tenen alguns inconvenients, com ara la utilització de quantitats relativament grans de dissolvents orgànics i que els procediments per aplicar-les són llargs. Per aquest motiu, durant l'última dècada, l'atenció s'ha centrat en el desenvolupament de

tècniques de microextracció que són fàcils de realitzar i alhora redueixen el consum de dissolvents orgànics i el nombre d'etapes. El primer objectiu d'aquesta tesi ha estat el de revisar l'estat de l'art de les diferents tècniques de microextracció basades en l'ús de sorbents sòlids i la seva aplicació a la determinació de PPCPs en mostres aquoses d'interès ambiental. En aquesta revisió, es detallen els fonaments i les innovacions, recentment introduïdes, de tècniques com la microextracció en fase sòlida (SPME), la microextracció per sorció en barra magnètica agitada(SBSE), la microextracció per sorció en barra d'agitació (SRSE), la microextracció en disc rotatori (RDSE), la microextracció d'adsorció en barra (BAμE) i l'extracció amb varetes de silicona (SR) o tubs de silicona (ST), així com els seus principals punts forts i febles. Tot i que totes aquestes tècniques tenen un gran potencial, hi ha una clara necessitat de desenvolupar mètodes menys costosos i més senzills que es basin en l'ús de materials a granel, ex. varetes de silicona. Els materials basats en vareta polidimetilsiloxà (PDMS) presenten eficiències similar a les que s'obtenen amb SBSE i compleixen els requisits analítics de puresa, ser inertsi d'estabilitat tèrmica. Altres avantatges dels SR són la seva flexibilitat i robustesa, juntament amb el fet que el seu baix cost fa que siguin d'un sol ús, eliminant els problemes associats a l'efecte memòria. El segon objectiu d'aquesta tesi va ser desenvolupar un nou mètode analític per a la determinació de NAP, KET, CBZ, DCF, TCS i MPB en aigües superficials basat en la seva extracció i preconcentració mitjançant una vareta de PDMS. Després de l'extracció, es procedia a la seva desorció amb un solvent orgànic líquid i a la seva determinació cromatogràfica per HPLC-DAD. Es van estudiar els diferents paràmetres i condicions que afecten a les etapes d'extracció (modificador orgànic, força iònica, cinètica i volum de mostra) i de desorció (dissolvent, volum, temps de desorció i aplicació de sonicació) d'aquests compostos en la vareta de PMDS.

El procediment desenvolupat consisteix en submergir una vareta de silicona de 10 mm (SR) en 50 mL d'una solució aquosa a pH 2 i NaCl 15%, l'extracció es duu a terme durant 10 hores (tota la nit) fins arribar a l'equilibri. Per l'etapa de desorció, es posa en contacte la vareta amb 200 μL de metanol durant 30 minuts en un bany d'ultrasons i seguidament es procedeix a l'anàlisi per HPLC-DAD. En aquestes condicions, es van obtenir factors d'enriquiment de 10 per NAP, 24 per KET, 108 per DCF i 179 per TCS, mentre que compostos més polars, CBZ i MPB no es van poder preconcentrar. Les eficiències obtingudes segueixen l'ordre d'hidrofobicitat dels analits i demostren que la barra de PDMS té més afinitat per compostos amb Kow> 3.

El mètode desenvolupat és senzill i permet l'ús d'instrumentació que actualment està disponible en la majoria de laboratoris analítics. Els límits de detecció es troben en el rang de 0,47 a 1,02 $\mu g.L^{-1}$, excepte 3,4 $\mu g.L^{-1}$ per CBZ i RSD%, que es troba en el rang de 0,4-9,7%. Els LODs assolits pel mètode desenvolupat són relativament bons i propers als d'altres tècniques de microextracció que utilitzenla mateixa tècnica instrumental. A més, molts dels sorbents utilitzats en les publicacions consultades no són comercials i s'han hagut preparar prèviament mitjançant processos sintètics més o menys complexes. Els LODs obtinguts en el mètode desenvolupat es poden millorar reduint el volum de desorció, tot i que aquesta reducció està limitada pel requeriment de que la vareta ha d'estar completament submergidaen el dissolvent de desorció, fent necessari l'ús de volums més grans i per tant, els factors d'enriquiment que s'obtenen no són tant grans. Una altre opció és la d'evaporar el metanol fins a sequedat i després reconstituir la solució amb un menor volum de dissolvent. Tanmateix, la combinació de la metodologia proposada basada en l'ús d'un SR comercial amb LC-MS/MS proporcionaria la sensibilitat suficient per a poder aplicar aquest mètode a la monitorització de NAP, KET, DCF i TCS en aigües superficials.
El mètode desenvolupat va ser validat mitjançant l'anàlisi de mostres d'aigua superficial fortificada a tres concentracions traça diferents obtenint-se recuperacions d'entre el 84,8 i el 111,2%. El mètode es va aplicar a l'anàlisi de mostres d'aigua de riu per a determinar NAP, KET, DCF, CBZ i TCS demostrant-se la seva viabilitat.

Com s'ha comentat anteriorment, les plantes convencionals de tractament d'aigües residuals (EDAR) són poc eficients en l'eliminació de la majoria dels microcontaminants orgànics. L'optimització del procés (per exemple, l'augment dels temps de residència de fangs), la coagulació-floculació i les tecnologies avançades, com l'osmosi inversa i l'ozonització i altres processos avançats d'oxidació (AOP), poden arribar a eliminar els microcontaminants de les aigües, tot i que el seu alt cost limita la seva utilització. A més, en el cas dels AOPs, es poden arribar a generar subproductes intermedis dels procés de degradació tòxics. Una alternativa menys costosa, senzilla i eficient és l'ús de processos d'adsorció, que permeten eliminar una gran varietat de compostos orgànics i metàl·lics de les aigües. El carbó actiu en forma granulada o en pols és un dels adsorbents més utilitzats atesa la seva elevada capacitat d'adsorció però el seu cost elevat i per tant, la necessitat de regenerar-lo, fa que el seu ús a gran escala sigui limitat. Una alternativa de baix cost al carbó actiu és l'ús de biosorbents com residus agrícoles, algues, biomassa fúngica, etc., que es poden utilitzar directament o modificar-los mitjançant tractaments físics o químics amb l'objectiu de millorar la seva

capacitat d'adsorció. Entre ells, els materials lignocel·lulòsicshan estat un dels més àmpliament estudiats per desenvolupar sorbents rendibles. El suro, un material hidrofòbic lignocel·lulòsic, està composat d'aproximadament un 45% de suberina i 27% de lignina, entre altres components, i pot interaccionar amb els contaminants orgànics mitjançant els anells aromàtics i els grups carbonil i hidroxil de la suberina i la lignina. La pols o els gränuls de suro són els principals subproductes de la indústria surera i s'han aplicat com a biosorbents per metalls pesants i altres microcontaminants com piretroïdes, fenols volàtils, paracetamol, cloroanisoles i hidrocarburs aromàtics policíclics (PAH).

El tercer objectiu d'aquesta tesi ha estat el d'avaluar la capacitat de sorció del suro granulat envers contaminants regulats com els compostos fenòlics, fenol (Ph), 2-clorofenol (2-CP), 2-nitrofenol (2-NP), 2,4-diclorofenol (2, 4-DCP), pentaclorofenol (PCP) i diclofenac (DCF) i contaminants emergents com el triclosan (TCS), el naproxén (NAP), ketoprofén (KET), carbamazepina (CBZ) i metil paraben (MPB). També es va estudiar l'efecte de diferents paràmetres, com ara el pH, la concentració i la quantitat de suro, sobre l'eficiència del procés d'adsorció. En les condicions més adients a pH 6 i partint d'una concentració inicial 30 $mg.L^{-1}$, s'han obtingut percentatges d'eliminació del 100% pel pentaclorofenol, el 75% per al 2,4-diclofenol, el 55% per al 2-nitrofenol, 45% pel 2-clorofenol, 20% pel fenol. L'adsorció de compostos fenòlics segueix la seqüència PCP> 2,4-DCP> 2-NP> 2-CP> Ph i aquesta seqüència és la mateixa als diferents pH (4, 6) i quantitats de suro (100 i 200 mg) utilitzades. Aquest resultat es deu al fet que els derivats fenòlics amb grups funcionals electroatrients en l'anell aromàtic actuen com a àcids de Lewis i que l'estructura aromàtica de la lignina es pot considerar com a base de Lewis. Per tant, com més gran sigui l'electronegativitat dels grups funcionals en l'anell aromàtic, major és el grau d'adsorció del compost. No obstant, es va observar una disminució significativa en el percentatge d'adsorció de compostos fenòlics per suro i en els valors d'adsorció a pH 11 a causa de la ionització dels derivats fenòlics quan pH>pKa. En aquest cas de PPCP, les capacitats d'adsorció van seguir el seu ordre d'hidrofobicitat: TCS i DCF> NAP> KET> CBZ i MPB amb percentatges d'eliminació del 100% per diclofenac sòdic, 100% per triclosan, 82% per naproxén, 57% per ketoprofén, 50% per la carbamazepina i 50% pel metil paraben amb petites quantitats de suro (5-10 mg) i partint d'una concentració 1 $mg.L^{-1}$. Les altes eficiències d'adsorció obtingudes s'expliquen per les interaccions de tipus hidrofòbicentre el suro i els contaminants orgànics que es complementen amb les interaccions π-π entre els grups aromàtiques d'aquests compostos i els anells aromàtics de la lignina. A més, la cinètica del procés d'adsorció de tots

els microcontaminants és relativament ràpida arribant-se a l'equilibri en menys de 30 minuts. Per caracteritzar el procés de sorció, les dades experimentals van ser analitzades amb les isotermes d'adsorció de Langmuir i Freundlich. Ambdós models s'adapten bé a les isotermes d'adsorció dels compostos fenòlics, mentre que en el cas dels PPCPs, només s'adapta a les dades experimentals el model Freundlich.

Les isotermes d'adsorció proporcionen informació pel procés d'escalat i permetencalcular la quantitat teòrica de suro necessària per a reduir les concentracions dels microcontaminants orgànics de 1 $mg.L^{-1}$ a 0,1 $mg.L^{-1}$. Les dosis teòriques varien entre 0,91 i 3,13 $g.L^{-1}$ per a NAP, KET, CBZ i MPB, que són valors relativament petits i que demostren que el suro és un sorbent eficient per a aquests compostos, així com també ho és per DCF i TCS, que van ser completament adsorbits, eficàcia del 100%, emprant només 5 mg de suro. El suro també és un adsorbent eficient per a l'eliminació de tots els compostos fenòlics estudiats i especialment per als compostos fenòlics més halogenats, PCP i 2,4-DCP, que només requereixen de dosis de 4,9 i 29 $g.L^{-1}$ de suro, respectivament, per reduir les seves concentracions en solucions aquoses de 1 a 0,1 $mg.L^{-1}$.

La capacitat d'adsorció del suro vers els compostos fenòlics i els PPCPs estudiats s'ha comparat amb els valors reportats en la literatura científica per a altres adsorbents. Per dur a terme aquesta comparació hem seleccionat carbó actiu produït a partir de deixalles vegetals i diversos residus agrícoles, ja que tenen un origen similar al suro. Atès que la capacitat d'adsorció depèn del pH de la solució, la quantitat i les característiques del sorbent, la concentració inicial dels compostos i el temps de contacte, és molt difícil comparar les capacitats de sorció de diferents adsorbents seleccionats amb els obtinguts amb el granulat de suro. En el cas dels compostos fenòlics, els valors d'adsorció obtingutsamb suro són més baixos que els reportats per biosorbents o carbonis tractats obtinguts a partir de biomaterials. Respecte a la sorció de PPCPs, hi ha molt pocs estudis amb residus vegetals no tractats i, en general, s'utilitza carbó actiu obtingut a partir de residus vegetals com a adsorbent. Els resultats obtinguts amb aquest tipus de carbó, concorda, en general, amb l'ordre de capacitats d'adsorció del nostre estudi i coincideix amb l'ordre d'hidrofobicitat dels mateixos.

L'ús del suro granulat o en pols com a biosorbent, presenta dues grans avantatges respecte altres biosorbents, un d'ells és que no requereix un pretractament previ i l'altre és que atès que es tracta d'un residu de la indústria surera, es pot adquirir a molt baix cost o es pot obtenir gratuïtament. Per a reduir els costos de transport, es pot utilitzar, preferentment, en plantes de tractament d'aigües residuals situades a prop de les indústries sureres.

Resumen

El control de la contaminación causada tanto por microcontaminantes orgánicos regulados y no regulados es de gran importancia ya que derivados fenólicos, productos farmacéuticos y de higiene personal se han detectado, a niveles de concentración traza, en los efluentes de entrada y salida de las depuradoras de aguas residuales. En el grupo de fármacos detectados, hay antiinflamatorios no esteroideos como el ketoprofeno (KTP) y el naproxeno (NAP), antiepilépticos, como la carbamazepina (CBZ) y analgésicos, como el diclofenaco sódico (DCF), y entre los productos de higiene personal, antisépticos como el triclosan (TCS) y conservantes, como el metilparabeno (MPB), todos estos compuestos se consideran contaminantes emergentes, ya que potencialmente pueden afectar a los ecosistemas acuáticos y la salud humana. Aunque la mayoría de estos compuestos no están regulados, el diclofenaco se ha incluido en la lista de contaminantes prioritarios de la UE y el TCS ha sido clasificado como contaminante de alta prioridad para la Agencia de Protección Ambiental (EPA) de Estados Unidos (USA). Los fenoles, que son disruptores endocrinos, también están en la lista de contaminantes prioritarios de la EPA. Teniendo en cuenta que las plantas de tratamiento de aguas residuales e industriales, no están diseñadas para eliminar microcontaminantes orgánicos y que además, muchos de estos compuestos son poco biodegradables, los efluentes de aguas residuales tratadas que los contienen son una de las fuentes principales de introducción de estos contaminantes en ríos y lagos que son reservorios de agua potable. Por lo tanto, hay que controlar la presencia de microcontaminantes orgánicos en las masas de agua dado sus posibles impactos ambientales asociados a su gran uso, frecuencia de detección y persistencia. Se han propuesto muchas metodologías analíticas para determinar las diferentes familias de microcontaminantes orgánicos, incluidos los fármacos e ingredientes de productos de higiene personal (PPCP), la mayoría de estos métodos se basan en el análisis de las aguas por cromatografía líquida con detección espectrofotométrica (Uv-vis) o por espectrometría de masas (MS). Las bajas concentraciones, $ng.L^{-1}$ o pocos $mg.L^{-1}$, de los microcontaminantes orgánicos en las aguas superficiales requiere de la aplicación de etapas de enriquecimiento y purificación de las muestras antes de su análisis cromatográfico, aunque se utilice la MS como técnica de detección. Se han desarrollado diversas técnicas de extracción y preconcentración para la extracción de analitos de muestras acuosas.Las técnicas convencionales de preparación de muestras son la extracción de líquido-líquido (LLE) y la extracción en fase sólida (SPE) que tienen algunos inconvenientes, como la utilización de cantidades relativamente grandes de disolventes orgánicos y que los procedimientos que se aplican son largos. Por este motivo,

durante la última década, la atención se ha centrado en el desarrollo de técnicas de microextracción que son fáciles de realizar y al mismo tiempo reducen el consumo de disolventes orgánicos y el número de etapas. El primer objetivo de esta tesis ha sido el de revisar el estado del arte de las diferentes técnicas de microextracción basadas en el uso de adsorbentes sólidos y su aplicación en la determinación de PPCP en muestras acuosas de interés ambiental. En esta revisión, se detallan los fundamentos y las innovaciones, recientemente introducidas, de técnicas como la microextracción en fase sólida (SPME), la microextracción por sorción en barra magnética agitada (SBSE), la microextracción por sorción en barra de agitación (SRSE), la microextracción en disco rotatorio (RDSE), la microextracción de adsorción en barra (BAμE) y la extracción con varillas de silicona (SR) o tubos de silicona (ST), así como sus principales puntos fuertes y débiles. Aunque todas estas técnicas tienen un gran potencial, hay una clara necesidad de desarrollar métodos menos costosos y más sencillos que se basen en el uso de materiales a granel, ej.varillas de silicona. Los materiales basados en varilla de poli-dimetilsiloxano (PDMS) presentan eficiencias similares a las que se obtienen con SBSE y cumplen los requisitos analíticos de pureza, ser inertes y de estabilidad térmica. Otras ventajas de los SR son su flexibilidad y robustez, junto con el hecho de que su bajo coste hace que sean de un solo uso, eliminando los problemas asociados al efecto memoria. El segundo objetivo de esta tesis fue desarrollar un nuevo método analítico para la determinación de NAP, KET, CBZ, DCF, TCS y MPB en aguas superficiales basado en su extracción y preconcentración mediante una varilla de PDMS. Tras la extracción, se procedía a su desorción con un solvente orgánico líquido y su determinación cromatográfica por HPLC-DAD. Se estudiaron los diferentes parámetros y condiciones que afectan a las etapas de extracción (modificador orgánico, fuerza iónica, cinética y volumen de muestra) y de desorción (disolvente, volumen, tiempo de desorción y aplicación de sonicación) de estos compuestos en la varilla de PDMS.

El procedimiento desarrollado consiste en sumergir una varilla de silicona (SR) de 10 mm en 50 mL de una solución acuosa a pH 2 y NaCl 15%, la extracción se lleva a cabo durante 10 horas (toda la noche) hasta llegar al equilibrio. Para la etapa de desorción, se pone en contacto la varilla con 200 □L de metanol durante 30 minutos en un baño de ultrasonidos y seguidamente se procede al análisis por HPLC-DAD. En estas condiciones, se obtuvieron factores de enriquecimiento de 10 por NAP, 24 para KET, 108 por DCF y 179 por TCS, mientras que compuestos más polares, CBZ y MPB no se pudieron preconcentrar. Las

eficiencias obtenidas siguen el orden de hidrofobicidad de los analitos y demuestran que la barra de PDMS tiene más afinidad por compuestos con K_{ow}> 3.

El método desarrollado es sencillo y permite el uso de instrumentación que actualmente está disponible en la mayoría de laboratorios analíticos. Los límites de detección son de 0,47 a 1,02 $\mu g.L^{-1}$, excepto 3,4 $\mu g.L^{-1}$ para la CBZ y RSD%, en el intervalo de 0,4 a 9,7%.

Los LODs obtenidos por el método desarrollado son relativamente buenos y similares a los de otras técnicas de microextracción que utilizan la misma técnica instrumental. Además, muchos de los adsorbentes utilizados en las publicaciones consultadas no son comerciales y se han preparado previamente mediante procesos sintéticos más o menos complejos. Los LODs se pueden mejorar reduciendo el volumen de desorción, aunque esta reducción está limitada por el requerimiento de que la varilla debe estar completamente sumergida en el disolvente de desorción, haciendo necesario el uso de volúmenes más grandes y por tanto, los factores de enriquecimiento que se obtienen no son tan grandes. Otra opción es la de evaporar el metanol hasta sequedad y después reconstituir la solución con un menor volumen de disolvente. Sin embargo, la combinación de la metodología propuesta basada en el uso de un SR comercial con LC-MS/MS proporcionaría la sensibilidad suficiente para poder aplicar este método a la monitorización de NAP, KET, DCF y TCS en aguas superficiales.

El método desarrollado fue validado mediante el análisis de muestras de agua superficial fortificada a tres valores de concentraciones traza diferentes obteniéndose recuperaciones de entre el 84,8 y el 111,2%. El método se aplicó al análisis de muestras de agua de río para determinar NAP, KET, DCF, CBZ y TCS demostrándose su viabilidad.

Como se ha comentado anteriormente, las plantas convencionales de tratamiento de aguas residuales (EDAR) son poco eficientes para eliminar la mayoría de los microcontaminantes orgánicos. La optimización del proceso (por ejemplo, el aumento de los tiempos de residencia de lodos), la coagulación-floculación y las tecnologías avanzadas, como la ósmosis inversa y la ozonización y otros procesos avanzados de oxidación (AOP), pueden llegar a eliminar los microcontaminantes de las aguas, aunque su alto coste limita su utilización. Además, en el caso de los AOPs, se pueden llegar a generar subproductos intermedios del proceso de degradación tóxicos. Una alternativa menos costosa, sencilla y eficiente es el uso de procesos de adsorción, que permiten eliminar una gran variedad de compuestos orgánicos y metálicos de las aguas. El carbón activo en forma granulada o en polvo es uno de los adsorbentes más

utilizados debido a su elevada capacidad de adsorción pero su elevado coste y por tanto, la necesidad de regenerarlo, hace que su uso a gran escala sea limitado. Una alternativa de bajo coste al carbón activo es el uso de bioadsorbents como residuos agrícolas, algas, biomasa fúngica, etc., que se pueden utilizar directamente o modificarlos mediante tratamientos físicos o químicos con el objetivo de mejorar su capacidad de adsorción. Entre ellos, los materiales lignocelulósicos han sido uno de los más ampliamente estudiados para desarrollar adsorbentes rentables. El corcho, un material hidrofóbico lignocelulósico, está compuesto de aproximadamente un 45% de suberina y 27% de lignina, entre otros componentes, y puede interaccionar con los contaminantes orgánicos mediante los anillos aromáticos y los grupos funcionales carbonilo e hidroxilo de la suberina y la lignina. El polvo o los gránulos de corcho son los principales subproductos de la industria del corcho y se han aplicado como bioadsorbentes por metales pesados y otros microcontaminantes como piretroides, fenoles volátiles, paracetamol, cloroanisoles e hidrocarburos aromáticos policíclicos (PAH).

El tercer objetivo de esta tesis ha sido el de evaluar la capacidad de adsorción del corcho granulado para con contaminantes regulados como los compuestos fenólicos, fenol (Ph), 2-clorofenol (2-CP), 2-nitrofenol (2-NP), 2,4-diclorofenol (2, 4-DCP), pentaclorofenol (PCP) y diclofenaco (DCF) y contaminantes emergentes como el triclosan (TCS), el naproxeno (NAP), ketoprofeno (KET), carbamazepina (CBZ) y metilparabeno (MPB). También se estudió el efecto de diferentes parámetros, como el pH, la concentración y la cantidad de corcho, sobre la eficiencia del proceso de adsorción. En las condiciones más adecuadas a pH 6 y partiendo de una concentración inicial 30 $mg.L^{-1}$, se han obtenido porcentajes de eliminación del 100% por el pentaclorofenol, el 75% para el 2,4-diclofenol, el 55% para el 2-nitrofenol, 45% para el 2-clorofenol, 20% por el fenol. La adsorción de compuestos fenólicos sigue la secuencia PCP> 2,4-DCP>2-NP> 2-CP>Ph en los diferentes pHs (4, 6) y cantidades de corcho (100 y 200 mg) utilizadas en el estudio. Este resultado se debe a que los derivados fenólicos con grupos funcionales electro-atrayentes en el anillo aromático actúan como ácidos de Lewis y que la estructura aromática de la lignina se puede considerar como base de Lewis. Por lo tanto, cuanto mayor sea la electronegatividad de los grupos funcionales en el anillo aromático, mayor es el grado de adsorción del compuesto. Sin embargo, se observó una disminución significativa en el porcentaje de adsorción de compuestos fenólicos por corcho y en los valores de adsorción a pH 11 debido a la ionización de los derivados fenólicos cuando pH>pKa. En este caso de PPCP, las capacidades de adsorción siguieron su orden de hidrofobicidad: TCS y DCF> NAP> KET> CBZ y MPB con porcentajes de eliminación del

100% para diclofenaco sódico, 100% por triclosan, 82% por naproxeno, 57% por ketoprofeno, 50% para la carbamazepina y 50% por el metilparabeno con pequeñas cantidades de corcho (5-10 mg) y partiendo de una concentración 1 $mg.L^{-1}$. Las altas eficiencias de adsorción obtenidas se explican por las interacciones de tipo hidrofóbico entre el corcho y los contaminantes orgánicos que se complementan con las interacciones π-π entre los grupos aromáticas de estos compuestos y los anillos aromáticos de la lignina. Además, la cinética del proceso de adsorción de todos los microcontaminantes es relativamente rápida llegándose al equilibrio en menos de 30 minutos. Para caracterizar el proceso de adsorción, los datos experimentales se analizaron con las isotermas de adsorción de Langmuir y Freundlich. Ambos modelos se adaptan bien a las isotermas de adsorción de los compuestos fenólicos, mientras que en el caso de los PPCPs, los datos experimentales sólo se adaptan al modelo de Freundlich.

Las isotermas de adsorción proporcionan información para el proceso de escalado y permiten calcular la cantidad teórica de corcho necesaria para reducir las concentraciones de los microcontaminantes orgánicos de 1 $mg.L^{-1}$ a 0,1 $mg.L^{-1}$. Las dosis teóricas varían entre 0,91 y 3,13 $g.L^{-1}$ para NAP, KET, CBZ y MPB, que son valores relativamente pequeños y que demuestran que el corcho es un adsorbente eficiente para estos compuestos, así como también lo es para el DCF y el TCS, que fueron completamente adsorbidos, eficacia del 100%, empleando sólo 5 mg de corcho. El corcho también es un adsorbente eficiente para la eliminación de todos los compuestos fenólicos estudiados y especialmente para los compuestos fenólicos más halogenados, PCP y 2,4-DCP, que sólo requieren de dosis de 4,9 y 29 $g.L^{-1}$ de corcho, respectivamente, para reducir sus concentraciones en soluciones acuosas de 1 a 0,1 $mg.L^{-1}$.

La capacidad de adsorción del corcho hacia los compuestos fenólicos y los PPCPs estudiados se ha comparado con los valores reportados en la literatura científica para otros adsorbentes. Para llevar a cabo esta comparación hemos seleccionado carbón activo producido a partir de desechos vegetales y varios residuos agrícolas, ya que tienen un origen similar al corcho. Dado que la capacidad de adsorción depende del pH de la solución, la cantidad y las características del adsorbente, la concentración inicial de los compuestos y el tiempo de contacto, es muy difícil comparar las capacidades de adsorción de diferentes adsorbentes seleccionados con los obtenidos con el granulado de corcho. En el caso de los compuestos fenólicos, los valores de adsorción obtenidos con corcho son más bajos que los reportados por biosorbentes o carbonos tratados obtenidos a partir de biomateriales. Respecto a la adsorción

de PPCP, hay muy pocos estudios con residuos vegetales no tratados y, en general, se utiliza carbón activo obtenido a partir de residuos vegetales como absorbente. Los resultados obtenidos con este tipo de carbón, concuerda, en general, con el orden de capacidades de adsorción de nuestro estudio y coincide con el orden de hidrofobicidad de los mismos.

El uso del corcho granulado o en polvo como bioadsorbente, presenta dos grandes ventajas respecto otros bioadsorbentes, uno de ellos es que no requiere un pretratamiento previo y el otro es que dado que se trata de un residuo de la industria del corcho, se puede adquirir a muy bajo coste o se puede obtener gratuitamente. Para reducir los costes de transporte, se puede utilizar, preferentemente, en plantas de tratamiento de aguas residuales situadas cerca de las industrias corcheras.

Summary

The control of contamination caused by both regulated and non-regulated micropollutants is of great importance as compounds such as phenol derivatives and pharmaceuticals and personal careproducts are detected in influent and effluent wastewater at trace levels. Pharmaceuticals including non-steroidal anti-inflammatory drugs such as ketoprofen (KTP) and naproxen (NAP), antiepileptics, such as carbamazepine (CBZ), and analgesics, such as sodium diclofenac (DCF) and personal care products, including antiseptics, such as triclosan (TCS), and preservatives, such as methyl paraben (MPB) are classified as emerging contaminants as they are regarded as possible threats to the aquatic environment and human health. Although these compounds are normally not regulated, Diclofenac has recently been included in the EU priority contaminant list [1] and TCS has been categorized as a high priority pollutant by the Environmental Protection Agency (EPA). Phenols, which are endocrine disruptor compound, are also included in the EPA priority list of pollutants. Given that micropollutants are not target compounds of industrial and sewage treatment plants, these contaminants are normally not eliminated due to their poor biodegradability and therefore are able to make their way into sources of drinking water such as river waters and lakes However, it is necessary to control the presence of organic micropollutants in water bodies because of their potential environmental impacts: frequent occurrence, persistence and risk to aquatic life and humans. Many analytical methodologies have been proposed to measure trace levels of organic micropollutants, including PPCPs, most of them are based on liquid chromatography analysis with ultraviolet (UV-vis) or mass spectrometry detection [2]. Trace level concentrations of PPCPs in environmental waters require the application of sample enrichment steps prior their chromatographic analysis even if the most sensitive MS detection is used. Several extraction and preconcentration techniques have been developed for the extraction of analytes from aqueous samples. Conventional sample preparation techniques are liquid-liquid extraction (LLE) and solid-phase extraction (SPE). However, these techniques have some drawbacks, such as time-consuming procedures or the use of large amounts of organic solvent. For these reasons, over the last decade, attention has focused on the development of miniaturized extraction techniques (microextraction techniques), that are easy to perform and reduce the need for organic solvent consumption and multistage operations, The first objective of this thesis was to revise the state of art of sorptive microextraction techniques and their applications for the determination of PPCPs in environmental liquid samples. The principles and innovations of solid-phase microextraction (SPME), stir-bar

sorptive extraction (SBSE), stir-rod-sorptive extraction (SRSE), and novel sorptive microextraction techniques such as bar adsorptive microextraction (BAμE) and silicone rod(SR) / silicone tube (ST) extraction are described as well as their main strengthens and weakness. Although all these techniques have great potential, there is a clear need for less costly and simpler methods such as the use of bulk materials e.g. silicone rods. PDMS rod-based materials present similar efficiencies to that obtained by SBSE and meets analytical requirements in terms of purity, inertness and thermal stability. Other advantages of SRs are their greater flexibility and robustness, together with the fact that they can be discarded after a single use, eliminating problems of carry over. The second objective of this thesis was to develop a new analytical method for the determination of NAP, KET, CBZ, DCF, TCS and MPB based on their extraction and preconcentration by PDMS rod. This step was followed by liquid desorption and high performance liquid chromatography (HPLC)-DAD analysis. The conditions affecting the extraction (organic modifier, ionic strength, kinetics and sample volume) and desorption (solvent, volume, desoption time, and the application of sonication) of these compounds from the PDMS rod were studied.

Finally, a 10 mm-silicone rod (SR) was immersed in 50mL of a sample solution containing 15% NaCl at pH 2 allowing extraction to take place overnight. A sonication-assisted desorption is then performed by putting SR in contact with 200 µl of methanol for 30 min before HPLC-DAD analysis. In these conditions, enrichment factors of 10 for NAP, 24 for KET, 108 for DCF and 179 for TCS were obtained whereas CBZ and MPB were not preconcentrated. The efficiencies follow the hydrophobicity order of the target analytes and showing that the PDMS rod has the highest affinity to compounds having log K_{ow}> 3.

The method developed is simple and allows the use of instrumentation that is currently available in most analytical laboratories. The detection limits are in the 0.47 to 1.02 $\mu g.L^{-1}$ range, except 3.4 $\mu g.L^{-1}$ for CBZ, and RSD%, which is in the 0.4–9.7% range. The LODs achieved by the developed method are relatively as good and near as those of other microextraction techniques using the same instrumental system. Furthermore, most of the sorbent phases reported in the literature are not commercially available and were previously synthesised. The LODs obtained in the method developed here can be improved by reducing the desorption volume, although this reduction is limited by the need for the SR to be completely immersed in the desorption solvent that makes it necessary to use greater volumes, or by evaporating the methanol extract until dryness and then reconstituting the solution with a lesser volume of solvent. For instance, the combination of the proposed methodology based

on the use of a commercial SR with LC-MS/MS will result in a suitable method having sufficient sensitivity as to be applied in the monitoring of NAP, KET, DCF and TCS in surface waters.

The developed method was validated by analysing spiked surface water samples at trace levels resulting in recoveries of between 84.8 and 111.2%. The application of the developed method to the analysis of real water samples has demonstrated its feasibility to determine NAP, KET, DCF, CBZ and TCS in river water.

The majority of micropollutants have not been identified as targets of conventional wastewater treatment plants (WWTPs). Process optimization (e.g. increasing sludge residence times), coagulation-flocculation and advanced technologies, such as reverse osmosis and ozonation and other advanced oxidation processes (AOP), are able to remove micropollutants from water, although their high cost limits the degree to which they are employed and, in the case of AOP, toxic intermediate by-products can be generated. A less costly, simple and efficient alternative is the use of adsorption processes, which are able to remove a variety of metallic and organic compounds from aqueous systems. Given its high adsorption capacity, granulated or powdered activated carbon has become the most widely used adsorbent. However, the need to constantly regenerate spent carbon makes this material costly also in scaled-up use. A low-cost alternative to activated carbon is the use of biosorbents, including agriculture wastes, seaweed, fungal biomass, etc., which uptake capacities can be improved by physical or chemical modification. Among them, lignocellulosic materials have been widely studied to develop cost efficient sorbent materials. Cork, a lignocellulosic hydrophobic material, is composed of approximately 45% suberin and 27% lignin, among others components and can interact with organic pollutants by the aromatic rings and carboxyl and hydroxyl groups of suberin and lignin. Cork powder and granules is the major sub products of the cork industry and have been applied as biosorbent for heavy metals and other micropollutants such as pyrethroids, volatile phenols, paracetamol, chloroanisoles and polycyclic aromatic hydrocarbons (PAHs).

The third objective of this thesis was to evaluate the sorption capacity of granulated cork towards regulate phenolic compounds (phenol (Ph), 2-chlorophenol (2-CP), 2-nitrophenol (2-NP), 2,4-dichlorophenol (2,4-DCP), pentachlorophenol (PCP), and diclofenac (DCF)) and emerging contaminants (triclosan (TCS), naproxen (NAP), ketoprofen (KET), carbamazepine

(CBZ), and methyl paraben (MPB). The effect of several parameters, such as pH, compound concentration, and amount of cork on the efficiency of the adsorption process was also studied. Maximum removal percentages of 100% for pentachlorophenol, 75% for 2,4-diclhorophenol, 55% for 2-nitrophenol, 45% for 2-chlorophenol, 20% for phenol were obtained for a 30 mgL^{-1} solution at pH 6. The adsorption of phenolic compounds follows the sequence PCP> 2,4-DCP> 2-NP > 2-CP >Ph and this sequence is the same at the different pHs (4, 6) and amounts of cork (100 and 200 mg) tested. This result is due to the fact that the phenolic derivatives with electronegative substituting groups in the aromatic ring act as Lewis acids and that the aromatic structure of lignin can be viewed as Lewis bases. Therefore, the greater the electronegativity of the substituting groups in the aromatic ring, the greater the extent to which the given compound is adsorbed. However, a significant decrease in the percentage of adsorption of phenolic compounds by cork and in the uptake values were observed at pH 11 due to the increase in the concentration of the ionized organic forms when pH>pKa. In this case of PPCPs, the adsorption capacities followed their order of hydrophobicity: TCS and DCF>NAP>KET> CBZ and MPB with removal percentages of 100% for sodium diclofenac, 100 % for triclosan, 82% for naproxen, 57% for ketoprofen, 50% for carbamazepine, and 50% for methyl paraben when small amounts of cork (5-10 mg) and 1 mgL^{-1} solution were used. The high removal efficiencies obtained are explained by the hydrophobic interactions of cork with organic pollutants that are complemented by the π–π interactions between the aromatic moieties of the compounds and the aromatic rings of lignin. Moreover, the adsorption process was almost complete after 30 minutes for all the micropollutants. In order to characterise the sorption process the experimental data were analysed by the Langmuir and Freundlich isotherm models. Both models fit well with the adsorption isotherms for phenolic compounds whereas in the case of PPCPs, the Freundlich model only fits the experimental data.

Adsorption isotherms provide information for the scaling process allowing the theoretical cork dosage required to reduce the organic micropollutant concentrations from 1 $mg.L^{-1}$ to 0.1 $mg.L^{-1}$, to be calculated. These dosages ranged from 0.91 to 3.13 $g.L^{-1}$ for NAP, KET, CBZ and MPB show that cork resulted to be an efficient sorbent for these compounds as well as for DCF and TCS, for which a 100% removal efficiency was obtained by using 5 mg of cork. Cork is also a useful adsorbent for the removal of all the phenolic compounds studied and especially for the more halogenated phenolic compounds, PCP and 2,4-DCP, which only require 4.9 and 29 $g.L^{-1}$ of cork, respectively, to reduce their concentrations in aqueous solutions from 1 to 0.1 $mg.L^{-1}$.

The adsorption capacity of cork towards phenolic compounds and PPCPs has been compared with those reported for other adsorbents. Among them, we selected activated carbon produced from vegetable wastes and various agricultural wastes, as these have a similar origin to cork. As the adsorption capacity depends on the pH of the solution, the amount and characteristics of the sorbent, the initial concentration of the target, and the contact time, it is very difficult to compare the sorption capacities of different adsorbents. For the sorption of phenolic compounds, the values obtained using cork are lower than those obtained with treated biosorbents or carbons obtained from biomaterials. Few studies have reported the sorption of PPCPs using non-treated vegetable wastes and, in general, activated carbons generated from vegetable wastes are used. In general, the results obtained with this type of carbons are in agreement with the adsorption capacity order obtained in this study.

The two great advantages of using granulated and powdered cork as an adsorbent are that, unlike other adsorbents, no pre-treatment is required and, given that it is currently treated as a waste product within the industry, it can be acquired for little or no cost. The cork residue can be used in wastewater treatment plants located near the cork industries resulting in reduced transportation costs.

Résumé

Le contrôle de la contamination causée par les micropolluants régulés et non régulés est d'une grande importance en tant que composés tels que les dérivés du phénol et les produits pharmaceutiques et de soins personnels sont détectés dans les eaux résiduaires à l'état de trace. Les Produits pharmaceutiques, tels que les médicaments anti-inflammatoires non stéroïdiens (le kétoprofène KTP) et du naproxène NAP), les antiépileptiques (la carbamazépine CBZ), les analgésiques (le diclofenac de sodium DCF), les produits de soins personnels (Le triclosan TCS) et les agents de conservation (le méthylparabène MPB), sont classés comme contaminants émergents car ils sont considérés comme des menaces potentielles pour l'environnement aquatique et la santé humaine. Bien que ces composés ne soient normalement pas réglementés, le Diclofenac a récemment été inclus dans la liste des contaminants prioritaires de l'UE [1] et le TCS a été classé comme un polluant hautement prioritaire par l'Environmental Protection Agency (EPA). Les phénols, qui sont des composés perturbateurs endocriniens, sont également inclus dans la liste prioritaire des polluants de l'EPA. Étant donné que les micropolluants ne sont pas des composés cibles des stations d'épuration industrielles et des stations d'épuration, ces contaminants ne sont pas éliminés en raison de leur faible biodégradabilité et peuvent donc pénétrer dans les sources d'eau potable telles que les rivières et les lacs. Cependant, il est nécessaire de contrôler la présence de micropolluants organiques dans les plans d'eau en raison de leurs impacts environnementaux potentiels: présence fréquente, persistance et risque pour la vie aquatique et les humains. De nombreuses méthodologies analytiques ont été proposées pour analyser les traces de micropolluants organiques, y compris les PPCPs; En effet les analyses peuvent être effectuées par chromatographie liquide avec détection par ultraviolet (UV-vis) ou par spectrométrie de masse [2]. Les concentrations à l'état de traces de PPCPs dans les eaux environnementales nécessitent l'application d'étapes d'enrichissement de l'échantillon avant leur analyse chromatographique même si la détection MS la plus sensible est utilisée. Plusieurs techniques d'extraction et de préconcentration ont été développées pour l'extraction d'analytes à partir d'échantillons aqueux. Les techniques conventionnelles de préparation d'échantillons sont l'extraction liquide-liquide (LLE) et l'extraction en phase solide (SPE). Cependant, ces techniques ont certains inconvénients, tels que des procédures qui prennent beaucoup de temps ou l'utilisation de grandes quantités de solvant organique. Pour ces raisons, au cours de la dernière décennie, l'attention s'est concentrée sur le développement de techniques d'extraction miniaturisées (techniques de microextraction), faciles à réaliser et réduisant le

besoin de consommation de solvants organiques et d'opérations multiétapes. Le premier objectif de cette thèse était de réviser l'état de l'art des techniques de microextraction sorptive et leurs applications pour la détermination des PPCPs dans des échantillons liquides environnementaux. Des nouvelles techniques de microextraction en phase solide (SPME), de l'extraction par sorption en barre d'agitation (SBSE), de l'extraction par sorption en tige d'agitation (SRSE) et des nouvelles techniques de microextraction sorptive telles que la microextraction par adsorption en barre (BAμE) et la microextraction par adsorption sur une tige en silicone (SR) ou sur une tube de silicone (ST) extraction sont décrits ainsi que leurs principales forces et faiblesses. Bien que toutes ces techniques aient un grand potentiel, il existe un besoin évident de méthodes moins coûteuses et plus simples telles que l'utilisation de matériaux en vrac, par ex. tiges de silicone. Les matériaux à base de barreaux PDMS présentent des rendements similaires à ceux obtenus par SBSE et répondent aux exigences analytiques en termes de pureté, d'inertie et de stabilité thermique. D'autres avantages des SR sont leur plus grande flexibilité et robustesse, ainsi que le fait qu'ils peuvent être jetés après une seule utilisation, éliminant ainsi les problèmes de report.

Le deuxième objectif de cette thèse était de développer une nouvelle méthode analytique pour la détermination de NAP, KET, CBZ, DCF, TCS et MPB sur la base de leur extraction et préconcentration par tige PDMS. Cette étape a été suivie par une désorption liquide et une analyse par chromatographie liquide à haute performance (HPLC)-DAD. Les conditions affectant l'extraction (modificateur organique, force ionique, cinétique et volume de l'échantillon) et la désorption (solvant, volume, désoption, et application de sonication) de ces composés sur la tige PDMS ont été étudiées.

Finalement, Une tige de silicone de 10 mm (SR) a été immergée dans 50 ml d'une solution d'échantillon contenant 15% de NaCl à pH 2 permettant l'extraction pendant une nuit. Une désorption assistée par sonication est alors réalisée en mettant en contact SR avec 200 μl de méthanol pendant 30 min avant l'analyse HPLC-DAD. Dans ces conditions, des facteurs d'enrichissement de 10 pour NAP, 24 pour KET, 108 pour DCF et 179 pour TCS ont été obtenus alors que CBZ et MPB n'étaient pas préconcentrés. Les efficacités suivent l'ordre d'hydrophobie des analytes cibles et montrent que la tige PDMS a la plus grande affinité pour les composés ayant un log Kow> 3.

La méthode développée est simple et permet l'utilisation de l'instrumentation actuellement disponible dans la plupart des laboratoires d'analyse. Les limites de détection sont comprises entre 0.47 et 1.02 $\mu g.L^{-1}$. Les limites de détection obtenues par la méthode développée sont

relativement bonnes et proches de celles des autres techniques de microextraction utilisant le même système instrumental. De plus, la plupart des phases de sorbant rapportées dans la littérature ne sont pas disponibles dans le commerce et ont été synthétisées auparavant. Les limites de détection obtenues dans la méthode développée ici peuvent être améliorées en réduisant le volume de désorption, bien que cette réduction soit limitée par la nécessité d'immerger complètement la tige de silicone dans le solvant de désorption nécessitant l'utilisation de volumes plus importants ou par évaporation du méthanol. Par exemple, la combinaison de la méthodologie proposée basée sur l'utilisation du tige de silicone commerciale avec LC-MS/MS aboutira à une méthode appropriée ayant une sensibilité suffisante pour être appliquée dans la surveillance de NAP, KET, DCF et TCS dans les eaux de surface.

La méthode développée a été validée en analysant des échantillons d'eau de surface dopés à l'état de traces. L'application de la méthode développée à l'analyse d'échantillons d'eau réels a démontré sa faisabilité de NAP, KET, DCF, CBZ et TCS dans l'eau de rivière.

La majorité des micropolluants n'ont pas été identifiés comme cibles des usines de traitement des eaux usées conventionnelles (SEEU). L'optimisation des procédés (par exemple, augmentation des temps de séjour des boues), La coagulation-floculation et les technologies avancées telles que l'osmose inverse et l'ozonation ainsi que d'autres procédés avancés d'oxydation (AOP) permettent d'éliminer les micropolluants de l'eau, bien que leur coût élevé limite la mesure dans laquelle ils sont employés et, dans le cas de l'AOP, des sous-produits intermédiaires toxiques peuvent être générés. Une alternative moins coûteuse, simple et efficace est l'utilisation de procédés d'adsorption, qui sont capables d'éliminer une variété de composés métalliques et organiques des systèmes aqueux. Compte tenu de sa capacité d'adsorption élevée, le charbon actif granulé ou pulvérisé est devenu l'adsorbant le plus largement utilisé. Cependant, la nécessité de régénérer constamment le carbone usé rend ce matériau coûteux également dans une utilisation à grande échelle.
Une alternative à faible coût au charbon actif est l'utilisation de biosorbants, y compris les déchets agricoles, les algues, la biomasse fongique, etc., dont les capacités d'absorption peuvent être améliorées par des modifications physiques ou chimiques. Parmi eux, les matériaux lignocellulosiques ont été largement étudiés pour développer des matériaux sorbants rentables. Le liège, un matériau hydrophobe lignocellulosique, est composé d'environ 45% de subérine et 27% de lignine, entre autres composants et peut interagir avec les

polluants organiques par les cycles aromatiques et les groupes carboxyle et hydroxyle de la subérine et de la lignine. La poudre et les granules de liège sont les principaux sous-produits de l'industrie du liège et ont été utilisés comme biosorbant pour les métaux lourds et d'autres micropolluants tels que les pyréthroïdes, les phénols volatils, le paracétamol, les chloroanisoles et les hydrocarbures aromatiques polycycliques (PAHs).

Le troisième objectif de cette thèse était d'évaluer la capacité de sorption du liège granulé des composés phénoliques (phénol (Ph), 2-chlorophénol (2-CP), 2-nitrophénol (2-NP), 2,4-dichlorophénol (2 ,4-DCP), le pentachlorophénol (PCP) et quelques produits pharmaceutiques tels que le DCF, le TCS, le NAP, le KET, le CBZ) et le MPB). Les taux d'élimination maximum sont de 100% pour le pentachlorophénol, 75% pour le 2,4-diclhorophénol, 55% pour le 2-nitrophénol, 45% pour le 2-chlorophénol, 20% pour le phénol pour une solution de 30 $mg.L^{-1}$ à pH 6.

L'adsorption des composés phénoliques suit la séquence PCP> 2,4-DCP> 2-NP> 2-CP> Ph et cette séquence est la même aux différents quantités de liège (100 et 200 mg) et pH (4, 6) testé. Ce résultat est dû au fait que les dérivés phénoliques avec des groupes de substitution électronégatifs dans le cycle aromatique agissent comme des acides de Lewis et que la structure aromatique de la lignine peut être considérée comme des bases de Lewis. Par conséquent, plus l'électronégativité des groupes de substitution dans le cycle aromatique est grande, plus le degré auquel le composé donné est adsorbé est grand. Cependant, une diminution significative du pourcentage d'adsorption des composés phénoliques par le liège et des valeurs d'absorption a été observée à pH 11 en raison de l'augmentation de la concentration des formes organiques ionisées lorsque le pH> pKa.

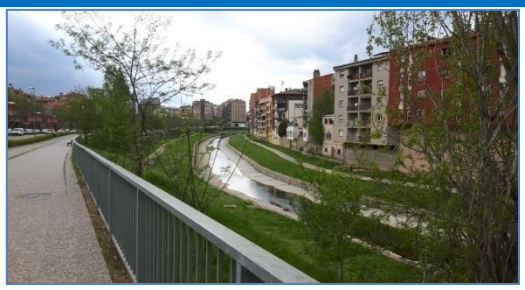
Les capacités d'adsorption suivent leur ordre d'hydrophobicité: TCS et DCF> NAP> KET> CBZ et MPB avec des pourcentages d'élimination de 100% pour le diclofénac sodique, 100% pour le triclosan, 82% pour le naproxène, 57% pour le kétoprofène 50% pour la carbamazépine et 50% pour le méthylparabène lorsque de petites quantités de liège (5-10 mg) et 1 $mg.L^{-1}$ de solution ont été utilisées. Les rendements élevés d'élimination obtenus sont expliqués par les interactions hydrophobes du liège avec les polluants organiques qui sont complétés par les interactions π-π entre les parties aromatiques des composés et les cycles aromatiques de la lignine. De plus, le processus d'adsorption était presque complet après 30 minutes pour tous les micropolluants. Afin de caractériser le processus de sorption, les données expérimentales ont été analysées par les modèles isothermes de Langmuir et Freundlich. Les deux modèles s'accordent bien avec les isothermes d'adsorption pour les

composés phénoliques, tandis que dans le cas des PPSP, le modèle de Freundlich ne correspond qu'aux données expérimentales.

Les isothermes d'adsorption fournissent des informations pour le processus d'entartrage permettant le dosage en liège théorique nécessaire pour réduire les concentrations en micropolluants organiques de 1 $mg.L^{-1}$ à 0.1 $mg.L^{-1}$, à calculer. Ces doses vont de 0.91 à 3,13 $g.L^{-1}$ pour NAP, KET, CBZ et MPB montrent que le liège s'est avéré être un sorbant efficace pour ces composés ainsi que pour DCF et TCS, pour lesquels une efficacité d'élimination de 100% a été obtenue en utilisant 5 mg de liège. Le liège est également un adsorbant utile pour l'élimination de tous les composés phénoliques étudiés et en particulier pour les composés phénoliques plus halogénés, PCP et 2,4-DCP, qui ne nécessitent respectivement que 4,9 et 29 $g.L^{-1}$ de liège pour réduire leurs concentrations dans des solutions aqueuses de 1 à 0,1 $mg.L^{-1}$. La capacité d'adsorption du liège vis-à-vis des composés phénoliques et des PPCPs a été comparée à celles rapportées pour d'autres adsorbants. Parmi eux, nous avons sélectionné le charbon actif produit à partir de déchets végétaux et de divers déchets agricoles, car ils ont une origine similaire au liège. Comme la capacité d'adsorption dépend du pH de la solution, de la quantité et des caractéristiques du sorbant, de la concentration initiale de la cible et du temps de contact, il est très difficile de comparer les capacités de sorption de différents adsorbants. Pour la sorption des composés phénoliques, les valeurs obtenues avec le liège sont inférieures à celles obtenues avec les biosorbants traités ou les carbones obtenus à partir de biomatériaux. Peu d'études ont rapporté la sorption de PPCPs utilisant des déchets végétaux non traités et, en général, des charbons actifs générés à partir de déchets végétaux sont utilisés. En général, les résultats obtenus avec ce type de carbones sont en accord avec l'ordre de capacité d'adsorption obtenu dans cette étude.

Les deux grands avantages de l'utilisation du liège granulé et pulvérisé comme adsorbant sont que, contrairement aux autres adsorbants, aucun prétraitement n'est requis et, étant donné qu'il est actuellement considéré comme un déchet dans l'industrie, il peut être acquis pour un coût minime ou non. Le résidu de liège peut être utilisé dans les usines de traitement des eaux usées situées à proximité des industries du liège, ce qui réduit les coûts de transport.

1. INTRODUCTION



Most of the water organic contaminants such as pesticides, industrial compounds, pharmaceuticals, personal care products, steroid hormones, drugs of abuse, and others has an anthropogenic origins [3]. Industries, agriculture and the general population release many contaminants into wastewaters as a result of their use of water.

The high population growth coupled with industrial and agricultural activities resulted in both an increased demand for clean water and the generation of high volumes of wastewaters. Urban wastewater treatment plants are generally designed to remove organic matter, nitrogen and phosphorous**,** but for organic micropollutants conventional treatment processes are not effective and many of these compounds are therefore discharged in surface waters where they may exert ecotoxicological effects at relatively low concentrations. The EU water framework directive 2000/06/CE listed 33 priority substances or groups of substances which include metals, pesticides, phthalates, polycyclic aromatic hydrocarbons, and endocrine disruptors that must be removed by wastewater treatments within an objective of quality and preservation of good ecological status of water in 2015 [4]. Groundwater, the largest body of fresh water in the European Union, has been identified to be also the most sensitive according to directive 2006/118/EC [5]. A wide range of organic pollutants have been detected in aquifers posing a risk to groundwater quality [6]. Thus, a proper assessment of water quality requires the identification of such regulated pollutants. Moreover, there are still some organic pollutants, that are still non-regulated although that research has provided growing evidence that many of them are endocrine disruptor compounds (EDCs) [7, 8] which are found in a wide range of products, including plastic bottles, detergents, flame retardants, food, toys, cosmetics, pesticides, etc. and are thought to have adverse developmental and reproductive effects in both humans and wildlife [9]. Different classes of micropollutants such as pharmaceuticals, drugs of abuse, surfactants and personal care products have been detected in wastewater treatment plant (WWTP) effluents [10] and secondarily terrestrial run-offs (from roofs, pavements, roads and agricultural land), including atmospheric deposition [5]. These compounds and their transformation products may be toxic and persistent and, despite being detected in low concentrations, may produce potentially harmful effects on ecosystems and human health [11], not to mention that the degradation products of some compounds such as alkyl phenols are even more toxic than the parent products [12].

Pharmaceuticals enter aquatic systems after ingestion and subsequent excretion in the form of the non-metabolized parent compounds or as metabolites through WWTPs [13]. On average WWTPs remove about 60–70% of the pharmaceuticals, but the removal of individual

compounds can vary between 0 and 100%. The remaining pharmaceuticals end up in surface waters, where they can adversely affect the aquatic environment and may cause problems for drinking water production [14]. Moreover, treated wastewater can be used for irrigation and PPCPs and phenolic compounds can reach terrestrial environments. Organic pollutants are introduced into the aquatic environment as illustrated in Figure 1.1:

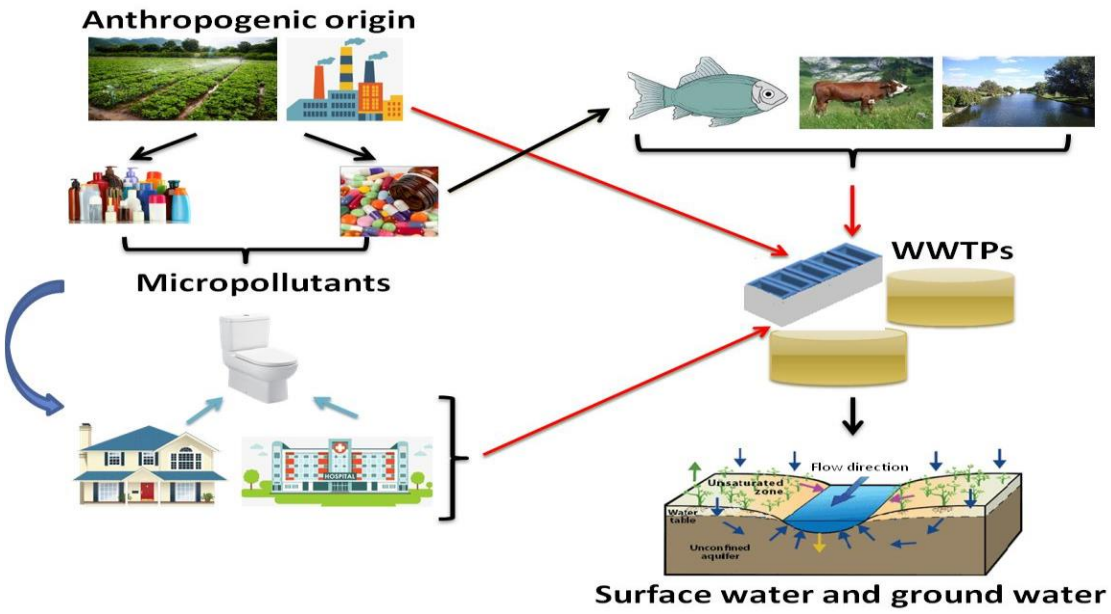


Figure 1.1. Origins and fate of organic micropollutants including pharmaceuticals and personal care products in the aquatic environment.

Organic chemicals can be volatilized, degraded, absorbed to sludge, or discharged in the aqueous effluent [15]. Therefore, it is interesting to be aware of the occurrence and fate of micropollutants in WWTP processes such as raw wastewater, effluent wastewater or sewage sludge and environmental water in order to evaluate the possible negative effects to aquatic and terrestrial organisms, and the possible migration of the compounds to surface and ground water. So, it is necessary to develop analytical methods which can detect and quantify the analytes at low levels in different and complex environmental samples.

Micropollutants consist of a vast and expanding array of anthropogenic as well as natural substances that are present in the aquatic environments at trace concentration levels. These include pharmaceuticals, personal care products, steroid hormones, industrial chemicals, pesticides and many other emerging compounds. In our study, we focus our attention on PPCPs and phenolic compounds which are illustrated in Figure 1.2.

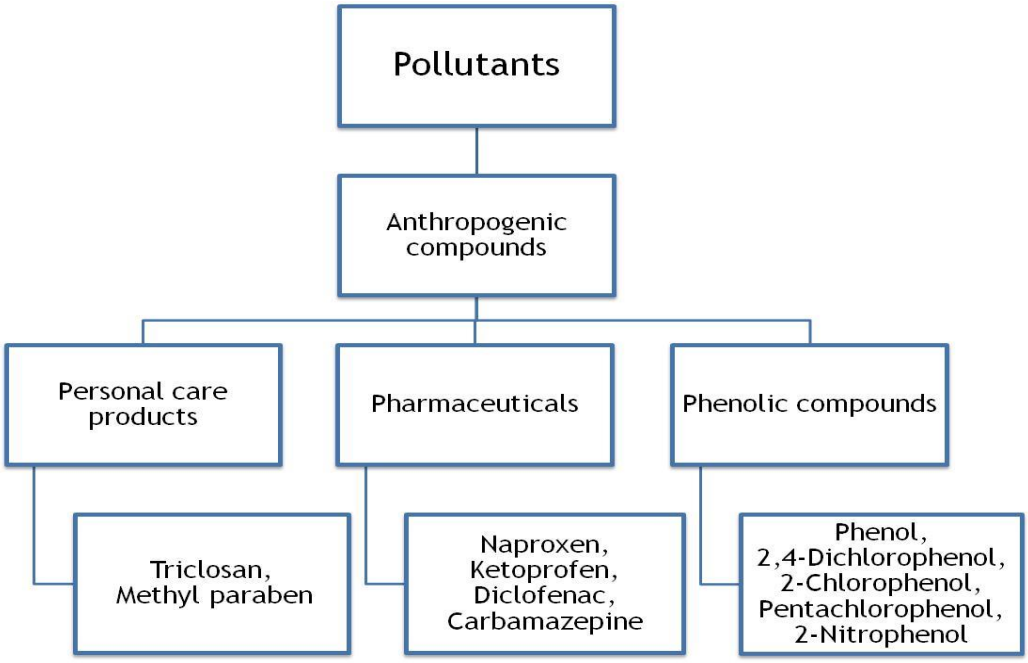


Figure 1.2. Classification of target micropollutants.

Pharmaceutical and personal care products (PPCPs) have been widely used in many fields such as medicine, industry, livestock farming, aquaculture, domestic and cosmetic use.

PPCPs are newly recognized classes of environmental pollutants that are receiving considerable attention due to the potential environmental impact: frequent occurrence, persistence and risk to aquatic life and humans. Although the occurrence of PPCPs is at trace levels in surface waters, from $ng.L^{-1}$ to $\mu g.L^{-1}$ [16-18], they can still affect water quality and ecosystem balance, and even affect drinking water resources [19].

Other contaminants such as phenolic compounds are also detected in these waters for the same reason. Moreover, phenolic compounds are present in many industrial processes and, as a consequence, they are also released in many industrial effluents. Phenols, which are endocrine disruptor compound (EDC), are listed in the US Environmental Protection Agency (EPA) priority list of pollutants and in EEC directive 76/464, related to dangerous substances discharged into aquatic environments [20].

Phenols and other EDCs are found in various products, including plastic bottles, detergents, flame-retardants, food, toys, cosmetics, and pesticides. These organic micropollutants and their degradation products may be toxic and persistent and, despite being detected in low concentrations, could produce potentially harmful effects on ecosystems and human health [21, 22].

In the following section, the main properties and characteristics of the different groups of microorganic pollutants are introduced. The organic compounds studied in this thesis can be classified into three types:

1) Pharmaceuticals, including non-steroidal anti-inflammatory drugs such as ketoprofen (KTP) and naproxen (NAP), antiepileptics, such as carbamazepine (CBZ), and analgesics, such as sodium diclofenac (DCF).

2) Personal care products, including antiseptics, such as triclosan (TCS), and preservatives, such as methyl paraben (MPB).

3) Phenolic compounds, such as phenol (Ph), 2-chlorophenol (2-CP), 2-nitrophenol (2-NP), pentachlorophenol (PCP) and 2,4-dichlorophenol (2,4-DCP).

In Table 1 the selected compounds, with some relevant physical-chemical properties, are presented.

1.1. Pharmaceuticals

Large amounts of pharmaceuticals are used for both therapeutic and veterinary purposes, and are eventually released into the environment. These products are usually designed to exert certain physiological effects on humans and livestock, but they can also adversely affect aquatic organisms [23]. More than 3,000 active substances are found on pharmaceutical products worldwide [24]. The groups of pharmaceuticals that are detected in aqueous samples worldwide include non-steroidal anti-inflammatory drugs, antidepressants, anti-epileptics, β-blockers, antibiotics, sedatives and contraceptives [25].

1.1.1. Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used drugs, primarily as analgesics, antipyretics and anti-inflammatory agents that are frequently detected in aquatic environments [26-29]. The most representative of these compounds are described below.

Table 1.1. Overview of the physical and chemical properties of the studied compounds.

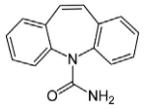
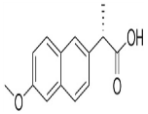
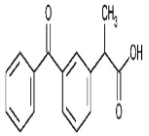
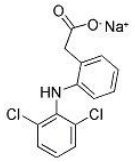
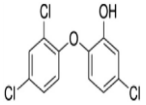
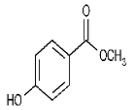
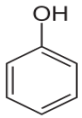
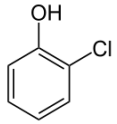
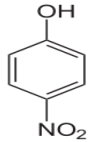
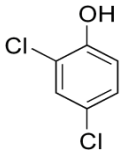
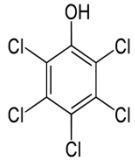
Compounds	Category	Chemical Structure	Physical-chemical properties			
			MW [a]	Sw[b]	pKa[c]	$LogK_{ow}$[d]
CBZ	Anticonvulsant		236.28	0.0177	13.9	2.45
NAP	non-steroidal anti inflammatory drug (NSAID)		230.27	0.0159	4.15	3.18
KET	non-steroidal anti-inflammatory drug (NSAID)		254.29	0.051	4.45	3.12
Sodium DCF	analgesic anti-inflammatory drug (NSAID)		318.13	2.37	4.3	3.91
TCS	Antiseptic		289.55	0.010	8.14	4.76
MPB	Preservative		152,15	2.45	8,4	1.93

Table 1.1. Overview of the physical and chemical properties of the studied compounds. (Continued)

Compounds	Category	Chemical Structure	Physical-chemical properties			
			MW [a]	Sw[b]	pKa[c]	Log K_{ow}[d]
Ph	Disinfectant		94.11	82.8	9.9	1.46
2-CP	paper, pesticide and herbicide production		128.56	22	8.56	2.15
2-NP	pesticides, wood preservatives, explosives		139.11	4.50	7.23	1.89 1.78
2,4-DCP	fungicide, herbicide, wood preservative		163.00	1.40	7.6	3.23
PCP	Pesticide		266.34	2.50	4.9 4.75	5.24 5.01

[a]Molecular weight ($g.mol^{-1}$).

[b] Water solubility (25 °C) ($g.L^{-1}$).

[c] Ionization constant (pKa).

[d] Octanol-water partition coefficient (logKow).

SRC physical properties database. Interactive Phys Prop Database Demo, 2009; <http://esc.syrres.com/interkow/physdemo.htm>.

1.1.1.1. Diclofenac (DCF)

Diclofenac (DCF) found as its sodium salt (diclofenac-Na), is used as an analgesic, anti-arthritic and anti-rheumatic drug. This compound is detected with average concentrations of 0.08 $\mu g.L^{-1}$ in effluent wastewater [30] with an influent concentration of 2.51 $\mu g.L^{-1}$ [31]. In environmental waters such as those of the Llobregat river (Spain) mean concentrations of DCF greater than 100 $ng.L^{-1}$ have been found [32]. It has been detected in surface waters in concentrations of 10 $\mu g.L^{-1}$ [33]. Diclofenac was included in Directive 39/2013/EU [1] due to its lack of biodegradability and the moderate potential for toxicity that it showed [34]. Recently, DCF has been included in the EU watch list of substances to be monitored in suface waters [35].

1.1.1.2. Naproxen (NAP)

Naproxen is a commonly prescribed acidic non-steroidal anti-inflammatory drug, which is not totally removed by conventional wastewater treatment plants due to its low biodegradability (degradation rate constant, K_{Biol}, from 1.0 to 1.9) [34]. It has been detected in surface waters in concentrations of 121 $\mu g.L^{-1}$ [33].

1.1.1.3. Ketoprofen (KET)

Ketoprofen is a commonly used NSAID, which is extensively used for the treatment of pain, fever, and inflammation, and is frequently detected in wastewater effluents and surface waters with concentrations ranging from $ng.L^{-1}$ to $\mu g.L^{-1}$ [36-38]. It has been detected in surface waters in concentrations of 102 $\mu g.L^{-1}$ [33].

1.1.2. Antiepileptic

1.1.2.1. Carbamazepine (CBZ)

Carbamazepine is an antiepilepticand mood stabilising drug used to control seizures and for the treatment of trigeminal neuralgia and some psychiatric diseases (e.g., bipolar disorders). It has attracted particular attention in recent years due to its widespread detection in effluent wastewaters [39, 40], surface waters [41], and drinking waters [42]. It is also noted to be highly resistant to biodegradation and thus recalcitrant under standard biological wastewater treatment conditions [40]. It was classified as potentially harmful compound for aquatic organisms by Council Directive 92/32/EEC [43]. CBZ was considered to be toxic to various

aquatic organisms including invertebrates, bacteria, fish, and algae [44]. It is one of the most persistent drugs in the environment and had been identified in various water bodies with concentrations of 0.01–2 $mg.L^{-1}$ [45, 46].

1.2. Personal care products

Personal care products (PCPs), including preservatives (e.g. parabens), disinfectants (e.g. TCS), insect repellents (e.g. DEET), fragrances (e.g. musks), and sunscreen UV filters (e.g. 4-methyl-benzylidene-camphor (4-MBC)), are typically used for the enhancement of living standards [33]. PCPs have received increasing attention as emerging contaminants due to their ubiquitous presence in the environment [47, 48].

1.2.1. Triclosan (TCS)

Triclosan (TCS) is a broad-spectrum antimicrobial compound that is often present in personal care and household products [49]. Due to its low biodegradability, TCS has been detected in effluent wastewaters [50], and surface waters [51] with concentrations up to 24 $\mu g.L^{-1}$ [52, 53]. The presence of TCS, which is already ubiquitous in the environment, is expected to increase in line with the increased use of TCS containing products [54]. TCS is reported to be highly bioaccumulative and has been reported as being an endocrine-disruptor [55, 56], causing skin irritation and susceptibility to allergies. Furthermore, it is toxic in aquatic and terrestrial environments [57] and can disrupt the nitrogen cycle in sensitive soils at certain concentrations [58]. In light of the growing concerns about the adverse effects of TCS on the environment, its removal from waters and wastewaters has become an important issue and has been identified as a high priority pollutant by the EPA in their aggregate risk assessment [2, 59].

1.2.2. Methyl paraben (MPB)

Methyl paraben (MPB), a widely used preservative, exhibits endocrine-disrupting properties with oestrogenic activity [60]. EPA has classified parabens as emerging environmental contaminants [61]. Despite the restricted threshold limit of these chemicals in cosmetics by the European Union, parabens and their residues have frequently been detected in rivers [53, 62], discharges of wastewater treatment plants and even in drinking water [63]. The amounts of methyl paraben (MP) in various cosmetic products are reported to be higher compared to others [64] and may cause breast cancer [65]. Parabens biodegrade in natural environments

although reaction rates are slow andeven more so when the alkyl chain length and the degree of chlorination increase [66]. The presence of parabens in the discharge of wastewater treatments plants (WWTPs) shows that removal through conventional treatment processes is incomplete [67]. It has been detected in surface waters of the European countries with concentrations of 1.7-1598 ng.L^{-1} [68].

1.3. Phenolic compounds

The use of pesticides plays an important role in harvest quality and food protection, providing enormous benefits in increasing production, as pests and diseases can have a devastating effect on crops [69]. The massive use of pesticides worldwide, and the difficulty in their degradation, has led to the spreading of pesticide residues throughout the environment as a result of atmospheric, terrestrial, subsurface and groundwater transport [70, 71]. Due to their inherent toxicity and persistence in the environment, the use of chlorophenols has recently been restricted or banned in several countries, such as Sweden, Finland, Germany and Singapore while they are still in use for wood-preservation in some other countries [72].

1.3.1. Phenol (Ph)

Phenol is a priority organic pollutant due to its harmful nature and poor biodegradability due to its relatively good solubility in water [73, 74]. Phenol, which has been shown to cause diarrhea and impaired vision in humans among other harmful effects [75], is found in the wastewater from different chemical industries, including pulp and paper, petroleum refinery, dye synthesis, coal gasification and the pharmaceutical industry [76]. The EPA set a maximum phenol concentration of 1 mg.L^{-1} in wastewater [77, 78].

1.3.2. 2-Chlorophenol (2-CP)

2-Chlorophenols are found in industrial wastewater as residues of the bleaching process in the pulp industry and can be present in the aquatic environment as a result of both hydrolysis and photolysis of chlorinated phenoxy acid herbicides [79]. 2-Chlorophenol is used in the manufacture of different compounds such as antiseptics, herbicides, dyes and other organic compounds [80]. 2-chlorophenol and other chlorinated compounds have been detected in wastewaters; moreover, most chlorinated phenols are found in municipal waste, agricultural run-off, leachates from polluted and contaminated sites, soil, water, sediments, air, food

products and body fluids [81]. It is listed as a priority pollutant by the EPA and by Decision n◦ 2455/2001/CE of the European Parliament [82, 83]. The reported levels of chlorophenols (CPs) in contaminated environments, range from 150 $g.L^{-1}$ to 100–200 $mg.L^{-1}$ [84].

1.3.3. 2-Nitrophenol (2-NP)

2-Nitrophenols and their derivatives, which are extensively used in the production of pharmaceuticals, synthetic dyes, and pesticides, are known to be serious environmental toxic, anthropogenic and biorefractory organic compounds which can cause serious damage to organisms and plants in the environment [85]. Due to their toxicological potential, nitrophenols have been considered as 'priority pollutants' by the EPA [86]. 2-nitrophenol was found to be especially toxic, and was of intense concern due to its high stability and solubility in water [87]. Therefore, in terms of environmental protection and food safety, there is an urgent need to develop simple and effective methods for the determination of NPs [88]. The EPA recommended the restriction of its concentration in natural waters to less than 4.8 $\mu g.L^{-1}$ [89].

1.3.4. 2,4-dichlorophenol (2,4-DCP)

2,4-dichlorophenol, one of the representative chlorophenols, is used in the production of herbicides (2,4-dichlorophenoxy acetate, etc.) and pesticides (pentachlorophenol, etc.). This pollutant is frequently found in industrial effluents, is regarded as having relatively high toxicity. Although its use has been restricted due to its carcinogenic properties, large amounts of wastewater containing this pollutant still drains into aquatic environments [90]. It is the 11^{th} of the 126 chemicals that have been designated as primary pollutants by the EPA [91]. Chlorophenols have been widespread in surface water, the concentrations for 2,4-dichlorophenol ranged from < 1.1 to 19960.0 $ng.L^{-1}$ have been detected [92].

1.3.5. Pentachlorophenol (PCP)

Pentachlorophenol (PCP) is one of the widespread environmental contaminants of soils, surface and ground water. PCP is a probable carcinogen and has been placed on the pollutant priority list of the EPA [93]. The main use of pentachlorophenol is as pesticides, a disinfectant and as a preservative of wood. PCP has a long-term harmful effect on the structure and functions of ecosystems even at very low concentrations and inhibits biodegradational processes in waters [94]. In general, the concentration levels in wastewaters were lower than

0.2 μg.L^{-1}, as set by Directive No 2008/150/EC (2008) [95] and < 3mg.L^{-1} in sewage and surface water [96].

The control of contamination caused by both regulated and non-regulated micropollutants is of great importance as compounds such as phenol derivatives and pharmaceuticals and personal care products are detected in almost all effluents. The determination of micropollutants in environmental samples is not an easy task due to the complexity of matrices and requires the use of analytical methods that are sufficiently sensitive as to permit trace level quantification.

1.4. Analytical methodologies

Analytical methods are used for product research and development, process control and chemical quality control purposes. Each step in the development of analytical methods must be fully understood to determine the extent to which environmental matrices and procedural variables affect the accuracy of the analysis in the different sample matrices [97].

Analyses of samples need several steps prior to performing analytical measurement, including:

- Identification of the analytical problem
- Sampling
- Pre-treatment of the sample
- Extraction and preconcentration of the analytes

The measurement is performed by using analytical instrumentation techniques that in the case of the determination of microrganic pollutants requires of the separation of the analytes prior their determination. Therefore, chromatographic techniques such as liquid chromatography (LC) with UV-vis or mass spectrometry (MS) detection, gas chromatography (GC) with mass spectrometry (MS)and tandem mass spectrometry-chromatographic techniques such as LC-M/M and GC-MS/MS are the most widely used techniques [98].

In the next sections, the main aspects of the different steps of the analytical process are explained.

1.4.1. Sampling, storage and pre-treatment.

The main objective of sampling is to obtain a representative portion of the total mass, which is treated in the laboratory for the determination of the analytes. Samples can be treated immediately at the site where the sampling takes place in order to avoid/minimise biological, chemical or physical changes that can occur between the time of collection and analysis, or stored appropriately. When storing, liquid and solid samples are normally frozen at -18ºC or refrigerated at 4ºC. The samples must be left to reach ambient temperature before analysis. In the determination of micropollutants in water samples, the filtration of the sample is a controversial step due to the risk of losing partially some of the analytes through a 0.45 μm filter.

1.4.2. Treatment of the sample

The basic concept of sample preparation is to convert a real sample into a sample suitable for analysis. Matrix effects are a major problem in extracting analytes [99].

Sample preparation prior to measurement by an analytical instrument is a time and labour-intensive step. The main objectives of sample preparation techniques are:

- To remove potential interferences from the sample matrix
- To convert the analytes into a more suitable form (e.g. via derivatization or pH adjustment);
- To increase the concentration of the target analytes
- To provide a robust, reproducible method that is independent of the sample matrix [99].

Although many traditional sample-preparation methods are still in use, there have been trends in recent years to achieve:

- The analysis of smaller initial sample sizes even in the case of trace analyses.
- Greater specificity and selectivity.
- Automation (on-line methods) in order to reduce manual operations.
- A more environmentally friendly approach with less waste and the use of only small volumes of organic solvents or none at all [100].

Sample preparation must also be tailored to the final analysis, taking into consideration the instrumentation to be used and the degree of accuracy required [99].

1.4.3. Extraction and preconcentration

Several extraction and preconcentration techniques have been developed for the extraction of analytes from aqueous samples. Conventional sample preparation techniques are liquid-liquid extraction (LLE) and solid-phase extraction (SPE). However, these techniques have some drawbacks, such as time-consuming procedures or the use of large amounts of organic solvent. For these reasons, over the last decade, attention has focused on the development of miniaturized extraction techniques. The main purpose of sample preparation is the elimination of interfering compounds from a matrix and, ideally, it should be simple, fast, selective, inexpensive and suitable for miniaturization [101]. New techniques such as solid-phase microextraction (SPME) [102] and stir-bar sorptive extraction (SBSE), that are easy to perform and reduce the need for organic solvent consumption and multistage operations, have been developed [103].

1.4.3.1. Liquid-liquid extraction (LLE)

LLE involves the distribution of analytes between two immiscible liquids. Although it is relatively simple to perform and manipulate, it does suffer from a number of drawbacks, including the large consumption of organic solvents, the high costs caused by spent solvent disposal, problems with inefficient phase separation due to emulsion formation. Another significant problem with LLE is the small preconcentration factors that can be achieved, mainly due to the difficulty of extracting large volumes of samples with small volumes of organic solvents. In general, LLE requires multistage operations to obtain a suitable enrichment factor [104]. LLE is a non-selective clean-up method based on the use of solvents including ethyl acetate, hexane, isooctane, toluene, chloroform and methylcyclohexane [105]. Despite this, it has been used for the extraction of pharmaceuticals, hormones and emerging contaminants [106, 107] in aquatic samples because of its simplicity and speed although SPE is preferred due to the absence of a number of drawbacks of LLE [105].

1.4.3.2. Solid phase extraction

The most widely used technique for the extraction of pesticides and PPCPs from water samples is solid phase extraction (SPE). SPE is a sorptive-based extraction technique in which a liquid sample flows through the solid-phase sorbent and the compounds are sorbed onto the surface of the sorbent. Then, a small volume of an appropriate organic solvent elutes the

retained analytes. SPE has a number of the advantages over LLE, including complete extraction of the analytes, more efficient separation of interferences from the analytes, the ability to process a small amount of sample, easier automation and, above all, the availability of different sorbents and formats that makes this technique suitable for the extraction of many compounds with different physicochemical properties from different matrices [108]. However, it is time-consuming and requires several steps (Figure 1.3), including washing, conditioning, sample loading, elution, and drying of the solid cartridge as well as sample pre-treatment procedures such as filtration to remove particulate matter and pH adjustment [109]. Each step of the SPE procedure is critically important to achieve a suitably concentrated and pure extract ready for instrumental analysis. As with chromatography columns, most SPE sorbents are either silica or polymer based. In order to obtain an efficient extraction resulting in pure and concentrated extracts, the sorbent used needs to have a high active surface area in order to shift the equilibrium in favour of the solid phase, so promoting analyte retention. The interaction between the analytes and the stationary phase should be suitably strong to allow for retention but easily reversed to guarantee a high degree of analyte recovery. The sorbent should be pure and free from impurities that may leach out and contaminate the extract and should allow for good contact between the sample and active groups [110].

Two basic approaches can be recognized when performing solid phase extraction, on-line and off-line, each of which has its advantages and limitations. The original off-line modification is simple and highly flexible. Therefore, it is often used in analytical research and in quick testing methods. On the other hand, the possibility of automation and the high sample throughput of on-line SPE are the major reasons for its growing use in routine target analyses and in analytical methods for continuous monitoring of water quality.

Moreover, different extraction modes can be applied in SPE for the clean-up and enrichment of the samples depending on the polarity and functional groups of the sorbent and analytes. Ion exchange mode is used for ionic analytes or analytes that can be converted to ionic form. In this mode, compounds are retained in a sorbent containing anion-exchange groups or cation-exchange groups. In normal phase mode, a polar sorbent is used for the extraction of polar compounds from a non-polar sample and the elution is carried out by a polar solvent which disrupts the polar interactions between the polar functional groups and the sorbent. Some possible sorbents are non bonded phases such as silica, alumina or magnesium silicate. In reversed phase mode, relatively non-polar compounds are separated from a polar phase such as water by a hydrophobic sorbent such as silica-based modified with C18 or C8 groups

and the elution is carried out with an organic solvent. In addition, different functional groups in the same sorbent can be used inducing different types of interactions in a mixed mode. ISOLUTE ENV+ (polystyrene-divinylbenzene based polymer with a hydroxyl group), Hydrophilic-lipophilic sorbents such as Strata X (polystyrene-divinylbenzene based polymer with a pyrrolidone group) and Oasis HLB (N-vinylpyrrlidone-divinylbenzene) are chemically modified sorbents with polar functionality that have acceptable capability for extracting low to moderate polar organic contaminants.

Molecularly imprinted polymers (MIPs) are another type of polymer with a «memory» of the shape and the functional groups of a template molecule. This material is designed in order to recognize selectively the template molecule used in the imprinting process, even in the presence of compounds with structure and functionality similar to those of the template. Most of the MIP sorbents were prepared in-house [111].

Nevertheless, various SPE sorbents including reversed-phase hydrophobic/hydrophilic balanced (HLB) polymeric sorbents, alkyl-modified silica (C-18 non-polar phase) and molecular imprinted sorbents have been applied among others for the determination of PPCPs [112]. HLB-based sorbents are the most preferred sorbents due to the improved recoveries and good extraction efficiency for PPCPs [113]. These sorbents are advantageous because they are stable in wide pH ranges, have no silanol interactions and they are not affected on drying the sorbent. HLB sorbents are able to retain acidic, basic, and neutral analytes [114]. Different multi-residue methods have been developed with Oasis HLB for the determination of pharmaceuticals and personal care products in environmental waters [115-117].

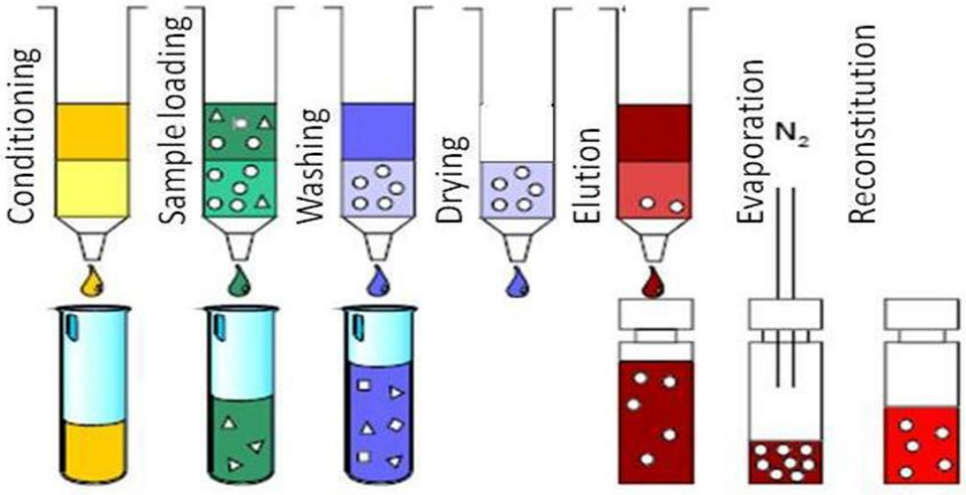


Figure 1.3. Solid phase extraction (SPE) steps.

1.5. Microextraction techniques

Recently, a great effort has been made to develop new analytical methodologies able to perform direct analyses using miniaturised equipment, thereby achieving high enrichment factors, minimising solvent consumption and reducing waste. These microextraction techniques improve the performance during sample preparation, particularly in complex water environmental samples.

Microextraction techniques are generally defined as non-exhaustive sample preparation methods that utilise a very small volume of the extracting phase (in the range of μL) relative to the sample volume [118]. Analytes are extracted using a small volume of a solid sorbent lthrough solid-phase microextraction (SPME) or of a liquid through solvent microextraction (SME). Both methods are useful alternatives for sample preparation due to their simplicity, effectiveness, low cost, minimal solvent use and their ability for an effective clean up the samples. Moreover, high enrichment factors can be achieved allowing, in some cases, the use of less sensitive detection techniques to be used [119].

Over the last two decades, a number of microextraction techniques have continuously been developed. The microextraction techniques are divided into two types: liquid-phase and solid-phase [120]. Figure 1.4 shows a classification of the microextraction techniques and the different formats that have been developed for analytical applications.

Liquid-phase microextraction techniques are divided into two formats: single drop microextraction (SDME) and membrane-assisted extraction techniques using hollow fibre (HF), membrane bag and flat sheet membrane. SDME is divided into two formats: direct immersion (DI) and headspace (HS) extraction. In most cases, SDME involves two-phase extraction, but three-phase extraction is also possible. Solid-phase microextraction techniques are also divided into two formats: sample stir microextraction and sample flow microextraction. In sample stir microextraction, SPME is the most dominant format and classified into static and flow-through formats. The static procedures are carried out by stirring the sample with sorbent material coated in fibre SPME, thin film micro extraction and SBSE. SPME is the most popular format in all techniques in which the sorbent may be either DI into the sample (DI-SPME) or exposed to HS in a closed container (HS-SPME). In the case of flow microextraction technique, in-needle SPME and in-tip SPME modes have been developed as an alternative to the in-tube SPME.

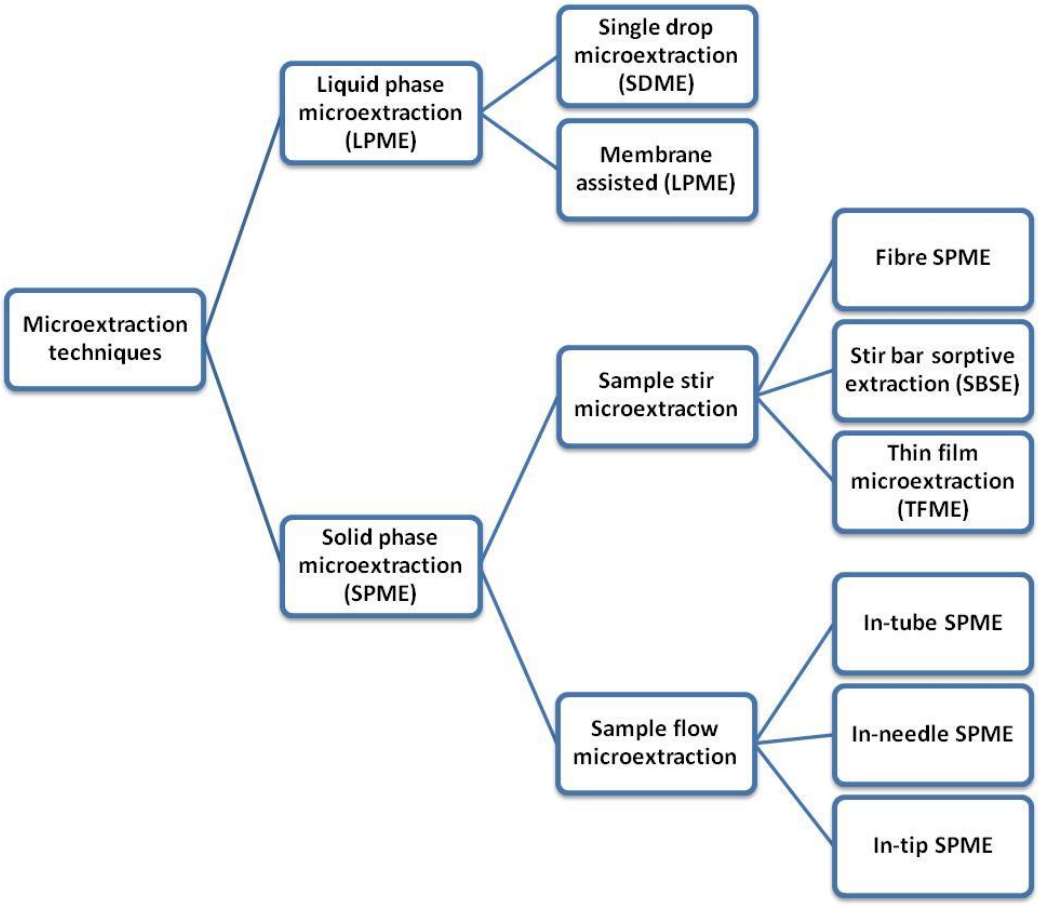


Figure 1.4. Classification of microextraction techniques.

One of the objectives of this thesis is to review the state of art of sorptive microextraction techniques, such as SPME and SBSE as well as novel sorptive extraction techniques such as bar adsorptive microextraction (BAμE) and silicone rod (SR) and silicone tube extraction (ST) and their applications toward the determination of PPCPs in environmental liquid samples.

1.6. Analytical determination

The determination of PPCPs in water samples at very low concentration levels (μg.L^{-1} to ng.L^{-1}) at which these contaminants are present together with a high number of matrix components that may interfere requires of the application of a clean-up and preconcentration step that can be performed using the extraction techniques explained in the previous section in combination with efficient and reliable chromatographic and detection techniques that allows the determination of the target compounds at environmental levels.

The instrumental separation technique to be used depends on the physical and chemical properties of the target analytes. Gas chromatography (GC) and high performance liquid chromatography (HPLC) are the most widely used separation techniques in environmental analysis although capillary electrophoresis (CE) has also been reported for the determination of PPCPs in environmental waters. In HPLC a liquid mobile phase and a stationary phase placed in a column are used for the separation of the analytes. The sample is transported to the column by the mobile phase where the analytes are retained and eluted after some time. Compounds with higher affinity for the stationary phase are more retained in the column, while compounds with low affinity are eluted faster. LC is used to determine polar, thermolabile and non-volatile compounds, while GC, which is based on the partition of the analyte between a stationary phase and a gaseous phase, is applied for non-polar, volatile and thermostable compounds. However, GC can be also applied to the determination of substances having low volatility and polarity by performing a derivatization prior to GC analysis. For phenolic compounds, the vast majority of published methods use gas chromatography separation. However, since phenolic compounds are polar, a derivatisation step is required to convert the compounds into non-polar derivatives. Different derivatisation strategies can be considered depending on the nature of the target compound and the extraction and determination technique employed. Derivatisation can be performed *in-situ* or *in-tube*. In the first case derivatisation occurs in the aqueous sample before, or simultaneously with, the extraction step. In the second case the derivatisation takes places after the extraction in the GC injection port. There are three basic types of derivatization reactions: alkylation, acylation and silylation. A GC-MS method was developed by Kawaguchi et al. [121] for the determination of BPA, PCP, NP and OP with acetylation derivatisation. The more frequently reactions used in in-tube derivatization are silylation with e.g. bis (trimethylsilyl) trifluoroacetamide (BSTFA) and esterification with diazomethane or pentafluorobenzylbromide. Different detectors can be used in gas chromatography, flame ionization (FID), thermal conductivity (TCD), and electron capture (ECD) or nitrogen phosphorus detector (NPD), among others. Electron capture detector (ECD) can also be used as these compounds are halogenated such as chlorophenols [122-125] that can be also analysed by GC-FID [126].

Mass spectrometer detectors (MS) coupled to a gas chromatograph instrument have become widely used for the analysis of environmental samples although in some cases MS detectors are less sensitive than some conventional ones. Two different ionization sources have

commonly been used for the determination of PPCPs in environmental waters, namely electron impact (EI) and chemical ionization (CI). The EI source is the most widely used ionization technique in GC-MS and GC-MS/MS analysis. In single MS detectors, parent ions, formed in the ion source, are monitored for each compound, meanwhile in MS/MS detectors mass transitions (after fragmentation of the parent ion) can be monitored, improving the selectivity and sensitivity of the method. Phenolic compounds such as Ph, 2-CP and 2.4-DCP were determined in water samples by GC–MS [127-129].

LC can be classified in normal phase (NPLC) and reversed phase (RPLC). In reversed phase a non-polar stationary phase and a polar mobile phase are used whereas in normal phase is the opposite. Due to polarity of the compounds analysed, reversed phase with octadecyl C18-bondded or octyl C8 bonded silica are the most commonly stationary phase used for the determination of pharmaceuticals and personal care products. The mobile phase is usually composed of two phases: one is the aqueous phase with adjusted pH and other is an organic phase mainly using methanol, acetonitrile or a combination of these two solvents. For instance, in order to obtain sufficient retention for acidic analytes and reproducible retention times, the use of buffer mobile phase at an acidic pH is recommended [130, 131]. An alternative to conventional normal or reverse phase LC is hydrophilic interaction liquid chromatography (HILIC). This is phase LC or normal phase LC (for determining polar, hydrophilic and ionic analytes, which often requires the use of an ion pairing reagent. The mobile phase used in HILIC is less hydrophilic than the stationary phase, in contrast to RPLC. The mobile phase in HILIC is mainly based on anorganic-aqueous mixture in which the initial state consists of a high percentage of organic solvents that decreases throughout the change in gradient. In the LC technique, as well as in the case of GC, different detection systems can be applied, such as ultraviolet-visible detector with a single wavelength (UV) or a diode array (DAD), in this last more than one wavelength can be monitored during the analysis, fluorescence (FL) and conductivity. MS detectors can also be coupled to LC through an interface, being this combination one of the most widely used today due to its universality and sensibility. Electrospray ionisation (ESI) is the interface commonly used for polar compounds due to its high sensitivity for this type of compounds while atmospheric pressure chemical ionisation (APCI) is used for medium-polarity and low-polarity compounds. In addition, when these interfaces are used, matrix effects can produce ion suppression or enhancement of the ion signal. The use of LC-MS/MS allows low detection limits to be achieved but the presence of matrix components in the samples may produce signal suppression or enhancement when

ESI is used. Furthermore, this technique needs to be performed by highly skilled technicians and requires the use of isotope-labelled compounds (ILC) as internal standards [132]. The use of preconcentration techniques such as those described in section 1.4.3 allows, in some cases, higher enrichment factors to be achieved and hence, conventional LC detectors such as UV-vis or DAD to be used given that the combination of the technique with an appropriate preconcentration technique increases the sensitivity and the selectivity of the analytical method.

The determination of phenolic compounds such as Ph, 2NP, 2CP, 2,4 DCP and PCP has been performed by LC with different detectors such as UV, DAD, EC, MS and tandem MS/MS [133, 134].

Pharmaceuticals are also widely determined by LC, due to the acidic character of some of these compounds. HPLC-DAD and liquid chromatography (LC) with ultraviolet (UV) detection methods were developed for the determination in environmental waters of acidic pharmaceuticals such as NAP, KET, NAP, CBZ and DCF [135-138]. TCS, which is a model for antibacterial compounds in personal care products, was determined by liquid chromatography (LC) with ultraviolet (UV) detection [139, 140].

LC-MS and LC-MS/MS methodologies were developed for the determination of pharmaceuticals in environmental waters. KET, NAP, DCF and TCS were determined by ion-pair liquid chromatography (IP-LC) tandem mass spectrometry MS [141]. However, LC–MS was applied for determination of DCF and CBZ [142]. On the other hand, KET, NAP, DCF, CBZ and TCS were determined by LC–MS/MS [143-146].

1.7. Removal of pollutants

As has been commented before, one of the biggest contributors of organic micropollutants in the environment are wastewater treatment plants (WWTPs) especially in the case of PPCPs as they are continuously introduced into sewage waters due to their large usage. Conventional wastewater treatments are not designed to remove micropollutants and, hence, the elimination of microrganic pollutants during conventional wastewater treatment processes is rather low as has been reported in several studies. Consequently, there is a growing need to develop reliable wastewater treatment methods, which enable an efficient removal of organic contaminants at trace levels avoiding their discharged to the aquatic environment though treated effluents. The capacity of biological treatment process adopted in urban WWTPs is conventional activated

sludge (CAS) to remove many of the organic pollutants. It has the capacity to remove the organic micropollutants from the wastewater, but the removal efficiency of them changed greatly, and varied with the physiochemical properties of compounds as well as environmental conditions such as the biological reactor configuration and operational parameters (hydraulic retention time, sludge retention time and pH) [16, 147]. In addition, negative mass balance where the effluent concentration is greater than the influent concentration has been reported in several cases.

1.7.1. Adsorption processes for the removal of organic micropollutants

Process optimization (e.g. increasing sludge residence times), coagulation-flocculation and advanced technologies, such as reverse osmosis and ozonation and other advanced oxidation processes (AOP), are able to remove micropollutants from water, although their high cost limits the degree to which they are employed and, in the case of AOP, toxic intermediate by-products can be generated [148]. A less costly, simple and efficient alternative is the use of adsorption processes, which are able to remove a variety of metallic and organic compounds from aqueous systems and that is widely used for drinking water purification. Adsorption implies the transference of the adsorbate from the fluid phase to the interfacial layer of the adsorbent and can involve physical and chemical interactions such as nonspecific dispersive interactions (e.g. van der Waals) and electrostatic interactions between ionic adsorbates and charged adsorbent surfaces [149].

The efficiency of the process depends of several factors including the characteristics of the adsorbent such as its chemical properties and porous structure, the chemical properties of the adsorbate and the pH, temperature and operational conditions [150].

Activated carbon (AC) is the most frequently used material because of its high porosity and specific surface area that makes AC very effective in removing a large number of contaminants being most effective for non-polar or moderately polar adsorbates. However, AC exhibits lower adsorption capacities for hydrophilic or polar compounds. In fact, sorption is together with biodegradation and volatilisation, one of the most significant processes in CAS, especially for organic contaminants with a log Kow > 4. Most of them such as some pesticides and PPCPs are poorly biodegradable during the CAS process.

Not with standing the high capacity of AC of removing organic contaminants at low concentration levels, the use of AC is limited by the high prices of commercial materials as well as for the high regeneration costs. Hence, attempts have been made to find out low-cost adsorbents that can be an alternative to activated carbon. Biosorption is an alternative

technology for the removal of a wide range of pollutants from aqueous systems. This technology entails using natural or engineered adsorbents derived from biomass for the removal of contaminants, and could be useful in the treatment of secondary or tertiary effluent [151]. Compared to conventional techniques such as ion exchange, coagulation and membrane separation, this approach has several advantages including low cost due to abundance of biomass, high selectivity, are regenerative and thus extend the life of waste materials, required less sophisticated operation skill, have limited sludge generation and generally have performance comparable to that of conventional techniques [152]. In developing countries, the application of biosorption for removal of organic contaminants is attractive for three reasons; (1) large quantities of biomaterials (e.g. crop residues, agro-processing wastes) for use as feedstock for biosorbents are readily available; (2) lack of advanced water and wastewater treatment systems for the removal of organic contaminants; and (3) the technology is relatively cheap compared to advanced methods (e.g. membrane filtration) often used in developed countries [153]. Ideally, biosorbents should require little pre-processing, be cost effective, be abundant in nature or is a by-product or waste material [154].

In the following sections, the main properties and characteristics of the different types of sorbents that are applied to remove organic micropollutants will be described.

1.7.2. Activated carbon

Activated carbon sorbents are tailored for specific applications mainly based on pore size and pore volume requirements. Porosity and other parameters are controlled by the following: raw material selection, activation process conditions, and post-processing steps. Depending on the application, activated carbon may be in the form of powder (PAC) (Figure 1.5), granule (GAC) or extrude (EAC). All three forms are available in a range of particle sizes. Most commercial activated carbons are manufactured from the following raw materials such as coal (anthracite, bituminous, sub-bituminous, lignite), coconut shell and wood. Less conventional raw materials such as peat, olive stones, fruit pits, petroleum coke, pitch, synthetic polymers, scrap tires and waste cellulose materials have also be employed to produce AC [155].

The activation may be chemical or physical. During chemical activation, initially the organic precursor is impregnated with different inorganics reagents (KOH, $ZnCl_2$, $FeCl_3$, H_3PO_4, etc.) and this mixture is pyrolysed in a conventional furnace [156] or in a microwave oven [157]. After the pyrolysis (under inert atmosphere), the inorganic contents are efficiently extracted

from the carbonized material, in order to produce activated carbons with high surface area [156-158]. For the thermal activation (physical activation) of the activated carbon, the carbon precursor is initially pyrolysed at 500–650°C under a N_2 flow, and then the temperature of the furnace is increased from 700°C to 1000°C, and kept in this temperature, changing the N_2 flow to CO_2 or CO_2 + H_2O [159]. The surface area of the activated carbons obtained ranges from 300 to 2500 $m^2.g^{-1}$ [158, 159]. The advantages of chemical activation are low energy cost due to lower temperature of process and higher product yield. Activated carbon prepared from chemical treatment of oil palm empty fruit bunches has been utilized for the removal of Ph, 2,4-DCF, and 2,4,6-trichlorophenol [160].

Torrellas et al. reported the preparation of activated carbon, using peach stones as carbon source, followed by chemical activation with H_3PO_4. This adsorbent was successfully employed for the sorption of CAF, DCF and CBZ [161].

Activated carbon can be obtained from different waste and natural materials such as pine bark, sawdust and cork bark among others [162]. Granular activated carbon (GAC) obtained from coal, coconut and wood has been used to remove phenols such as 2,4-DCF [163], and high surface area carbon adsorbents have been synthesized from pine-sawdust and applied to NSAIDs sorption [164].

The adsorption capacity of activated carbon to PPCPs mainly depends on the hydrophobicity and charge of the PPCPs. Activated carbon shows a higher preference towards hydrophobic (log K_{OW}> 4), low molecular weight, slightly positively charged compounds (at pH=7–8) and compounds contain aromaticity and N-heterocycles [165]. It has been demonstrated in both laboratory and pilot-scale experiments that water matrix affects the adsorption of PPCPs by activated carbon [166, 167] as well as the contact time [168], pH and the surface structure of activated carbon [169]. Activated carbon-based technology is the preferred in EU countries as an upgrading option for WWTPs given that is able for removing 80% of micro pollutant content in municipal WWTP effluents [165].

Figure 1.5. Granular activated carbon (GAC).

1.7.3. Carbon-based sorbents: graphene, graphene oxide and carbon nanotubes

Graphene is a carbon allotrope having defined features favourable for various environmental applications. The carbon nanomaterial-graphene oxide is produced by the oxidation of graphite through a chemical process. The significance of graphene is due to its chemical, thermal, electrical and mechanical properties, inimitable morphology, and high specific surface area. Due to its strong binding of delocalized π-electrons with toxic pollutants, graphene has been used as a rapid adsorbent for pollutant removal [170]. When strong oxidizing agents are used to oxidize graphite, oxygenated functionalities are introduced in the structure of the graphite, which makes the material hydrophilic, and also expands the layer separation. Due to the presence of oxygen functionalities, graphene oxide can easily disperse in organic solvents, water, and different matrices.

The removal efficiency of PPCPs by graphene and graphene oxide varied with the physico-chemical properties of PPCPs as well as the pH and the contact time [171, 172].

The relatively high surface area, small size and large porosity of carbon nanotubes (CNTs) make also them promising adsorbents for the removal of many organic micropollutants [173, 174]. Among them, the removal of PPCPs such as KET,CBZ [175] and TCS [176] have been investigated.

1.7.4. Biosorbents

The direct use of biosorbents, including agriculture wastes, seaweed, fungal biomass, etc., is a low-cost alternative to activated carbon and their uptake capacities can be improved by physical or chemical modification of these biomaterials [177, 178]. Papermill sludge, activated sludge, fly ash, sawdust, bagasse pith, rice husk ash, jute fibres, rice bran ash, and brown algae have been applied to phenolic compounds removal as substitutes of GAC [179]. Among them, lignocellulosic materials, which are derived from plants, have been widely studied to develop cost-efficient sorbent materials for the removal of metals and phenolic derivatives [180]. Some of these natural materials, such as almond shells, have proved to be particularly efficient in adsorbing PCP (93%) [181] and pomegranate peel and banana peel are also efficient in adsorbing, 2,4-DCP and Ph, respectively [182, 183].

Few studies have reported the sorption of PPCPs using non-treated vegetable wastes and, in general, activated carbons generated from vegetable wastes are used. The sorption of NSAIDs by this type of activated carbons has been recently revised by Ahmed [184]. AC from pine sawdust and pine chip is efficient to adsorb NAP and DCF and the adsorption by olive waste cakes-AC can remove KET. Activated carbons from peach stones, cyclamen tubers and potato peel waste were highly effectives in adsorbing DCF [184, 185] as well as AC from cocoa shell [186] and AC from coconut shell applied to adsorb NAP and CBZ [187]. In addition, the sorption on activated carbon based sorbents is a very effective process in removing some PPCPs from wastewaters, however, their production and regeneration requires energy and, in most cases, the use of chemical products [184, 188]. The direct use of biosorbents can be a cost effectiveness alternatively as it is the case of the removal of DCF by Isabel grape bagasse [189] and CBZ by rice straw [188] and granular cork [190].

1.7.4.1. Cork

Cork powder and granules are the major subproducts of the cork industry. Cork is a renewable, being a natural and ecological material, consisting of the outer bark of the cork oak tree, known botanically as *Quercussuber L*. Cork harvest and subsequent transformation is one of the most important and sustainable industries in the Portuguese and Mediterranean region economies [154]. The traditional use of cork has been highly focused on stoppers for wine bottling as we can see in Figure 1.6, although cork industry produces a series of other materials that span from agglomerates to composites applied in a series of end products, e.g. thermal and acoustic insulation cork boards, flooring panels, etc. The manufacturing of these

cork-derived materials produces a set of by-products that have a limited value, as is the case of cork powder, granules of expanded corkboard, among many others. Cork, a lignocellulosic natural material, has been used as a biosorbent for pollutants, such as insecticides, uranium, volatile phenols, paracetamol, chloroanisoles, polycyclic aromatic hydrocarbons, and heavy metals. Cork has already been evaluated as precursor for the preparation of activated carbons [191].

Figure 1.6. Cork stoppers industry and granular.

1.7.4.2. Characteristics and Properties of cork

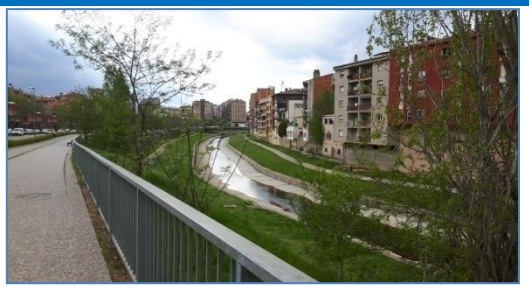
The make-up of cork is approximately 45% suberin, 27% lignin,12% polysaccharides, and 10% extractive compounds [154]. The adsorption capacity of cork is related to its physico-chemical properties and the adsorption mechanism depends on the presence of different type of functional groups in the cork surface. Cork granulates of 1-2 mm, such as those used in this study, have a surface area of 16.3 $m^2.g^{-1}$, a pore volume of 2.83 $cm^3.g^{-1}$ and a mean pore diameter of between 1-1.34µm, indicating the presence of macropores and that only the external surface area is available for sorption [192].

The interactions of cork with organic pollutants, which are essentially hydrophobic, are explained by the aromatic rings and carboxyl and hydroxyl groups of suberin and lignin. In the case of highly hydrophobic pesticides ($\log K_{ow} > 4$), such as chlorpyrifos, it has been established that raw cork is suitable for their retention. However, adsorption is less successful in the case of hydrophilic pesticides ($\log K_{ow} < 2$), such as methomylandoxamyl [193]. Moreover, the aromatic components of lignin interact with the aromatic moieties of the

adsorbed compounds via π-π interactions, as is the case in paracetamol and phenanthrene sorption [194, 195].

These findings have been confirmed by molecular modelling calculations, which reveal that π stacking, reinforced by hydrogen bonding, is the main contributor to the interaction between pesticides and lignin [193]. Granulated cork has also proved to be able to remove IBP, CBZ and clofibric acid (CA) from water and wastewater [190]. In this thesis we focus our attention on the adsorption of pharmaceuticals, cosmetic products and phenolic compounds by granulated cork.

2. OBJECTIVES



Given the harmful effects that organic contaminants such as phenolic compounds, pharmaceuticals and ingredients of personal care products have on ecosystems and human health, their distribution and fate in the environment needs to be monitored and effective removal processes must be developed to complement in wastewater plant treatments that are not designed to remove organic micropollutants. The monitoring of microrganic contaminants in the aquatic environment how they affect the quality of water is becoming increasingly important as consumption grows and their introduction into the environment remains unchecked. The main objectives of this thesis was to develop new simple, economical and environmentally friendly analytical methodologies, based on microextraction techniques for the determination of organic emerging pollutants in environmental waters and to evaluate the use of biosorbents such as cork for the removal of phenolic compounds and PPCPs from water. In the light of the aforementioned, the aims of this study were as follows:

1. To revise the different microextraction methodologies available for the extraction and preconcentration of PPCPs in water samples in order to examine the state of the art. In the light of this study, we identified the need to develop a new analytical method for the determination of PPCPs in natural waters.

2. The development of a simple and environmentally friendly new analytical methodology based on silicone rod (SR) microextraction combined with HPLC-DAD for the determination of diclofenac, naproxen, ketoprofen, carbamazepine, and triclosan in water samples including:

    a. The selection of the chromatographic and detection conditions.
    b. To study the different parameters affecting the extraction of the analytes (volume of solution, pH, addition of salt, modifiers, etc.) and the elution conditions (solvent, volume of desorption, time, etc.).
    c. To determine the analytical figures of merit and to validate the developed method through the analysis of spiked river water samples.
    d. To apply the developed analytical methodology to monitor PPCPs in river water samples.

3. The evaluation of the use of a sorption process for the removal of phenolic compounds (phenol, 2-chlorophenol, 2-nitrophenol, 2,4-dichlorophenol, and pentachlorophenol) in waters by using cork as a biosorbent.

    a. Investigation of the effect of variables such as pH, contact time, amount of sorbent and compound concentration on the sorption process.

    b. Characterization of the sorption process at equilibrium conditions by analysing the experimental data by the Langmuir and Freundlich adsorption isotherms models.

    c. Comparison of the adsorption model parameters obtained with cork as a biosorbent with those reported in the literature when other biosorbents are used.

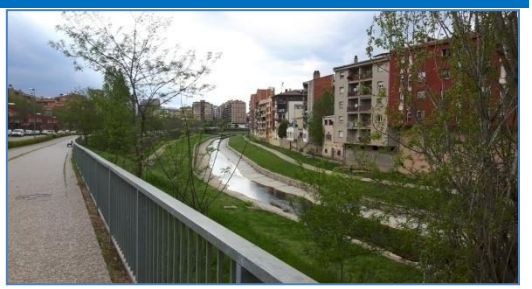
4. Evaluation of the ability of cork to adsorb PPCPs such as diclofenac, naproxen, ketoprofen, carbamazepine, methyl paraben and triclosan.

    a. Kinetics of the sorption process and effect of the amount of cork and compound concentration.

    b. Characterization of the PPCP sorption processes by applying Langmuir and Freundlich adsorption isotherms models to the equilibrium data.

    c. Comparison with other biosorbents and activated carbon-based biosorbents.

3. METHODOLOGY



The main objective of this thesis is to develop analytical methodologies based on chromatographic techniques for the determination of non-steroidal anti-inflammatory drugs such as naproxen, sodium diclofenac and ketoprofen, an antiepileptic and mood stabilising drug such as carbamazepine, and ingredients of personal care products such as triclosan, an antibacterial compound, and methyl paraben, a preservative. All of these compounds have been detected at trace levels in influent and effluent wastewaters as well as surface waters. Furthermore, another group of regulated contaminants, phenolic compounds (phenol, 2-chlorophenol, 2-nitrophenol, 2,4-dichlorophenol, pentachlorophenol) have also been studied in order to find out an efficient process to remove them from water. To this end, a biosorbent such as granulated cork has been evaluated to remove the above mentioned phenolic compounds as well as PPCPs at trace concentration levels. A serious of experiments were performed under controlled operating conditions and the adsorption process by which cork removes these contaminants has been characterised by analysing the experimental data using adsorption isotherm models. Most of the standards, reagents, apparatus and instruments used in the different experimental studies carried out in this thesis are the same so all them are described in a common section.

3.1. Standards and reagents

3.1.1. Pharmaceuticals and personal care products

TCS (5-chloro-2-(2,4-dichlorophenoxy) phenol), NAP ((2S)-2-(6-methoxynaphthalen-2-yl) propanoic acid), KET (2-(3-Benzoylphenyl) propanoic acid), CBZ (benzobenzazepine-11-carboxamide), MPB (methyl 4-hydroxybenzoate) and DCF sodium salt (sodium;2-[2-(2,6-dichloroanilino) phenylacetate) were purchased from Sigma–Aldrich (Germany).

A 500 $mg.L^{-1}$ stock solution containing each of the target compounds was prepared monthly in methanol and working solutions of PPCPs at a concentration of 10 $mg.L^{-1}$ were prepared by subsequent dilution of this stock solution in methanol or ultrapure water. The standard stock solution was stored in amber glass bottles and kept at 4°C in order to avoid degradation during the test period.

3.1.2. Phenolic compounds

Phenol 99.5%, 2-chlorophenol 99.5%, 2-nitrophenol 98.5 %, 2,4-dichlorophenol 99.5% and pentachlorophenol were from Dr. EhrenstorferGmh (Germany).

Individual stock solutions of 100 $mg.L^{-1}$ were prepared in ultrapure water by weighting the appropriate amounts of the solid compound in an analytical balance (Sartorius analytic, Spain). Working solutions ranging from 0.1 to 60 $mg.L^{-1}$ were prepared by dilution with ultrapure water.

3.1.3. Mobile phases

Chromatographic grade acetonitrile, provided by Fisher (USA), and methanol from Carlo Erba (Italy), were used for preparing the mobile phases and the solutions. Anhydrous sodium acetate, sodium hydroxide, 37% hydrochloric acid and acetic acid were from Sigma-Aldrich and sodium chloride from Carlo Erba (Italy). All chemicals used in this study were of analytical grade. NaOH and HCl solutions were used to adjust the pH of the test solutions. Ultrapure water with a conductivity of 18.2 MΩ/cm was obtained from a Millipore water purification system (Millipore, Express 40, USA).

The mobile phases were prepared in ultrapure water and filtered through a disposable 0.20µm nylon membrane filter (Whatman, Germany). The solutions were sonicated in an ultrasonic bath (J.P. Selecta, Spain).

3.2. Liquid chromatographic analysis

3.2.1. Phenolic compounds

The determination of the phenolic compounds was performed in a high performance liquid chromatograph (Spectra SYSTEM, ThermoQuest, Italy) consisting of an SCM1000 vacuum membrane degasser, a P2000 gradient pump, and a UV6000LP diode-array detector. Control and data processing were performed with ChromCard version 1.2 software (Thermo Quest, Italy). Chromatographic separation was achieved in a C18 reversed-phase column (5 µm, 20 x 0.46cm i.d., Teknokroma, Spain) with a guard column (5µm, 0.3 x 0.46cm i.d., Teknokroma, Spain) of the same packing material. The injection volume was set at 100 µL and the flow rate was 1 $mL.min^{-1}$. The mobile phase was an acetonitrile solution (CH_3CN:H_2O:CH_3COOH, 50:49:1) and the detection wavelength was set at 275 nm for Ph, 2-CP, and 2-NP, and at 286 nm for 2,4-DCP and PCP. In Figure 3.1 is represented a chromatogram of a 40 $mg.L^{-1}$ standard solution.

The calibration curves and LODs of this method are represented in Table 3.1.

Table 3.1. Figures of merit of the chromatographic method for the determination of Ph, 2-CP, 2-NP, 2,4-DCP and PCP.

Compounds	Retention time (min)	Equation of calibration curve	Linearity (R^2)	Linear interval ($mg.L^{-1}$)	LOD ($mg.L^{-1}$)	RSD (%) (n=6) 35 $mg.L^{-1}$
Ph	3.9	$Y = (1019 \pm 7)10^2X + (1 \pm 11)10^3$	0.999	1-40	0.2	0.6
2-CP	5.2	$Y = (1071 \pm 9)10^2X + (4 \pm 107)10^3$	0.999	1-40	0.3	0.5
2-NP	6.3	$Y = (296 \pm 1)10^3X + (8 \pm 50)10^3$	0.999	1-40	0.3	0.4
2,4-DCP	8.4	$Y = (93 \pm 1)10^3X + (-7 \pm 25)10^3$	0.999	1-40	0.5	0.7
PCP	15.6	$Y = (20 \pm 1)10^3X + (1 \pm 2)10^4$	0.999	5-40	2.0	1.5

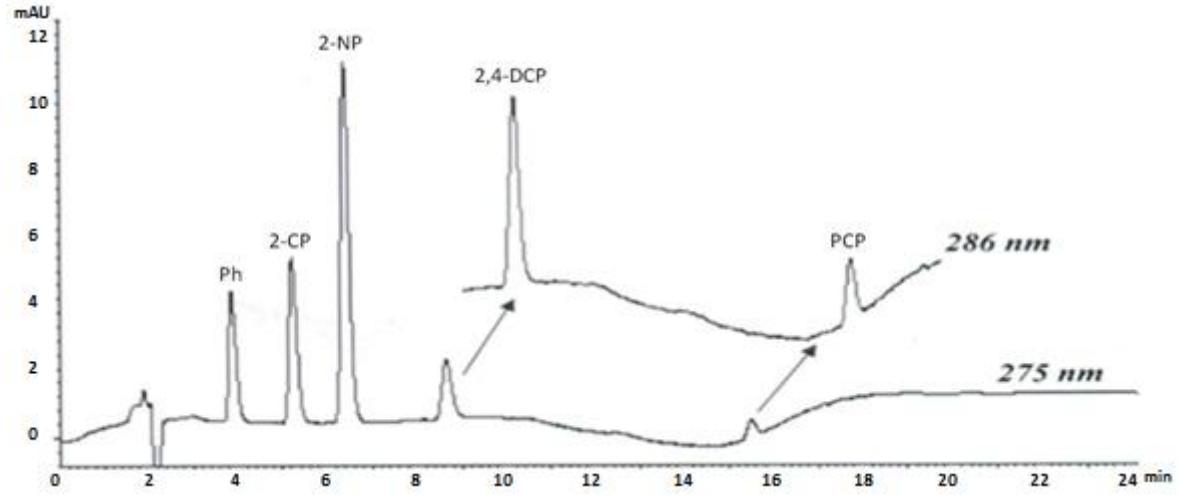


Figure 3.1. Chromatogram of a 40 mg.L^{-1} standard solution of phenolic compounds.

3.2.2. Pharmaceuticals and personal care products

An Agilent 1200 series high performance liquid chromatography system equipped (Figure 3.2) with two pumps (G13128), a degasser (G1379B), an autosampler (G1329B) and a DAD detector (G4212A) was used. System control and data acquisition were performed using Agilent ChemStation software. The analytes were separated in a C18 Luna column (50 × 2 mm, 2.5 µm) (Phenomenex, USA). The mobile phase, consisted of (A) Milli-Q water, 0.1% acetic acid and 0.3852 g of sodium acetate and (B) acetonitrile, was passed at a flow rate of 0.3 mL min^{-1} for the system in a gradient mode as follows: 0 min; 90% A, 5 min; 75% A, 15 min; 55% A, 20 min; 20% A, 23 min; 55% A, 25 min; 90% A. Total run time was 25 min. The detection wavelength was set at 242 nm for CBZ, NAP and TCS; 250 nm for KET and MPB, and 280 nm for DCF. In Figure 3.3 is represented a chromatogram of a 250 mg.L^{-1} standard solution.

The chromatographic separation and detection conditions for the chromatographic method are presented in Table 3.2.

Linearity was evaluated by extracting triplicate ultrapure water samples spiked at five different concentration levels ranging from 100 to 400 µg.L^{-1} of NAP, KET, CBZ, DCF, MPB and TCS (Table 3.2). The method was linear for all compounds and determination coefficients (r^2) were higher than 0.990.

Table 3.2. Figures of merit of the chromatographic method for the determination of NAP, KET, DCF, CBZ and TCS.

Compounds	Retentin time (min)	Equations of calibration curve	Linearity (R^2)	RSD interday (%) (n=6) **100**	**400**	RSD intraday (%) (n=6) **100**	**400**	LOD ($\mu g.L^{-1}$)	LOQ ($\mu g.L^{-1}$)
KET	12.93	$y = 0.998\,x + 0.607$	0.999	0.1	0.5	1.2	0.3	2.42	7.35
TCS	21.1	$y = 0.709\,x - 11.83$	0.998	1.3	1.9	0.6	0.5	5.45	16.76
NAP	13.58	$y = 2.272\,x + 0.614$	0.999	0.3	0.2	0.2	0.8	3.65	11.06
DCF	16.62	$y = 0.673\,x + 28.37$	0.999	1.1	0.4	0.3	0.3	3.99	12.11
CBZ	10.97	$y = 0.950\,x - 1.407$	0.999	0.2	0.5	0.8	0.3	4.48	13.6
MPB	7.631	$y = 1.699x - 1.320$	1	0.2	0.4	0.6	0.4	2.23	6.76

The LODs and LOQs were calculated using the Excel regression analysis tool and considering a signal-to-noise ratio of 3 and 10, respectively. LODs ranged from 2.23 to 5.45 $\mu g.L^{-1}$. LOQs ranged from 6.76 to 16.76 $\mu g.L^{-1}$. The precision of the method, expressed as RSD%, was evaluated by replicate analysis (n = 6) of ultrapure water samples spiked at two concentration levels (100 and 400 $\mu g.L^{-1}$). Intraday precision was in the range of 0.2–1.2% at both levels and interday precision was between 0.1 and 1.9%.

Figure 3.2. HPLC-DAD system used in the chromatographic analysis of PPCPs.

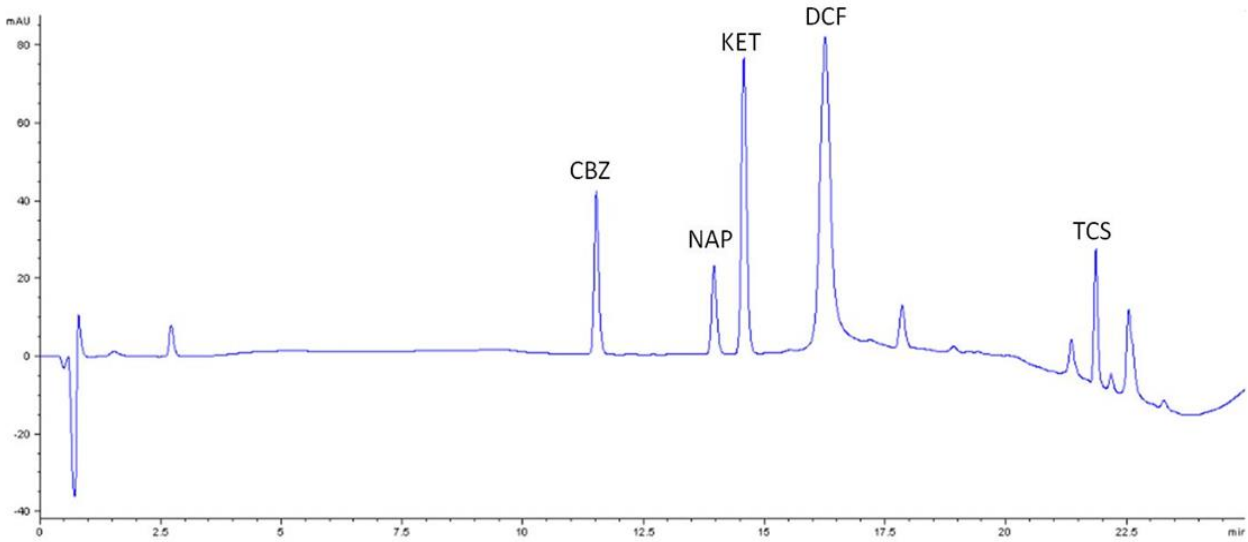


Figure 3.3. Chromatogram of a 250 $\mu g.L^{-1}$ standard PPCP solution in ultrapure water.

3.3. Development of analytical methodology based on silicone rod extraction.

The method is based on the extraction of pharmaceuticals and personal care products by commercial polydimethylsiloxane (PDMS) rods. The determination of all the studied compounds was carried out by high performance liquid chromatography with diode-array detection (HPLC-DAD). MPB was not added to the silicone rod (SR) method. The study of the different parameters affecting the extraction of the analytes and the elution conditions showed a slight decrease of concentration of desorption for MPB and it was not quantified.

3.3.1. PDMS rod extraction

Commercial 10 mm elastomer PDMS rods (appx. 0.037 g) (Goodfellow Cambridge, England) were cut from the PDMS cord. These were then cleaned and stored in methanol and, immediately prior to use, were dried with a lint-free tissue. Different experiments were performed to systematically study the conditions that can affect the extraction of the analytes (volume of solution, pH, ionic strength (addition of NaCl), organic modifiers) and the desorption (solvent, volume, desorption time and sonication). The results obtained are described in Chapter 4.

In a typical assay, the PDMS rod was immersed in 50mL of a solution containing 100 $\mu g.L^{-1}$ of each of the compounds in ultrapure water and 15% w/v of NaCl. The pH was then adjusted as required (2, 3, 6 and 9). The vial was then closed and the extraction was performed for different periods of time (3, 5, 8 and 10 h). Figure 3.4 shows the PDMS rod and the extraction process. The experiments were performed three times using a ten-point magnetic shaker (MultiMix D, Ovan, Spain) at 200 rpm. After extraction, the PDMS rod was removed with clean tweezers and then dried with a lint-free tissue. The rod was then placed into a tapered glass insert, Verex-EU vial (9 mm screw, 2 ml amber) (Phenomenex, USA), containing 200 µL of methanol. The vial was closed allowing the desorption process to take place. Desorption times of 15, 30 and 45 minutes with and without sonication were tested. The PDMS rod was removed and 10 µL of the extract was then injected into the liquid chromatograph.

Figure 3.4. PDMS rod and experimental set-up for the rod-based extraction process.

3.3.2. River water samples

In the experiments performed to study the matrix effect, river water samples were collected from the Onyarriver, (Girona, Spain) in 1 L amber glass bottles that had previously been rinsed in the river water. Samples were transported to the laboratory under refrigeration and then stored at 4°C. The samples were characterized by determining their conductivity, chemical oxygen demand (COD) and ionic composition [196]. The samples were filtrated using 0.45 μm nylon membrane filter (Millipore, USA). After filtration, the water samples were spiked with KET, NAP, DCF, CBZ, and TCS at different concentration levels (10, 25, 75 $\mu g.L^{-1}$) and recovery experiments were carried out in triplicate.

After validation, the developed method was applied to the analysis of water samples. Grab samples of surface water were collected in the Onyar, Ter and Fluvià rivers in Girona, Spain in 1L amber glass bottles. Samples were transported to the laboratory under refrigeration and then stored at 4ºC. The samples were then filtered with 0.45μm nylon membrane filters (Millipore, USA). All the experiments were carried out in duplicate.

3.4. Characterization of the adsorption process of organic contaminants by cork

We evaluated cork, a lignocellulosic natural material, as a biosorbent for the removal of pharmaceutical, personal care products and phenolic compounds from water. The analytical determination of these compounds was carried out by the HPLC-DAD methods described in section 3.2.

3.4.1. Cork

Granulated cork, kindly supplied by the Cork Centre (Palafrugell, Spain), was sifted to separate out powder particles of < 2 mm. The cleaning procedure consists of putting an amount of cork into contact with 10 mL of ultrapure water in 25 mL glass tapered tubes and placed in a horizontal rotatory mixer (DINKO, Spain) at 20 rpm for 30 min. After cleaning and air-drying the cork, it was put into contact with the test solutions. The batch adsorption experiments were conducted in duplicate at room temperature (20±2 °C).

3.4.2. Scanning electron microscopy (SEM)

The morphology of cork was observed by a scanning electron microscope (SEM) (Model ZEISS DSM-960A) (Figure 3.5). Samples were examined at a magnification range of 20 x to 500 x. Pictures of representative cork samples were taken and the particle size distribution was determined from these pictures.

Figure 3.5. Scanning electron microscopy (SEM).

3.4.3. Batch experiments

The experimental set-up is presented in Figure 3.6.

3.4.3.1. Phenolic compounds

After cleaning and air-drying the cork, it was put into contact with 10 mL of individual phenolic compound solutions. The initial concentration of the phenolic compounds was varied

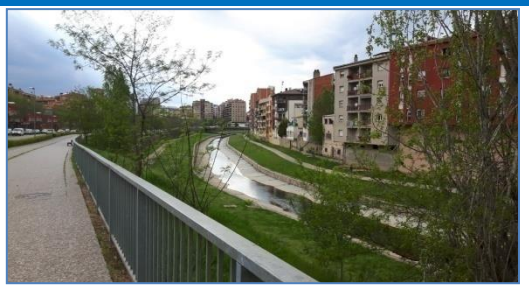
from 5 to 50 mg.L^{-1} and two amounts of granulated cork, 100 and 200 mg, were tested. The mixture was rotated until equilibrium was reached. The cork was then separated from the aqueous solutions by filtration through a 0.45 μm nylon filter (Merck Millipore, Spain) and the filtrate solution was analysed by the HPLC-DAD method described above. In order to establish the equilibrium time, various tubes containing a 30 mg.L^{-1} solution of the phenolic compounds and 200 mg of cork were agitated for different periods of time. The effect of the pH on sorption efficiency was studied at pH 4, 6 and 11 by adding the required volumes of 4 M HCl or 4 M NaOH solutions to the testing solutions.

3.4.3.2. Pharmaceuticals and personal care products

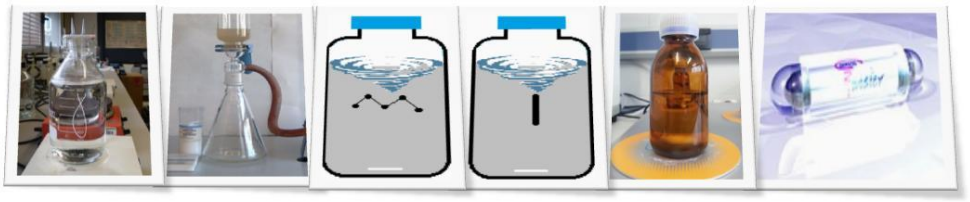
The performance of these experiments was limited by the low solubility of CBZ, NAP, KET, sodium DCF, TCS, and MPB in water (see Table 1) and by the high sorption capacity of cork towards these compounds. As a result, only a few milligrams of cork (5, 7.5, 10 and 20) and 20mL of trace concentrations (0.5 or 1 mg.L^{-1}) of the target compounds can be used in the batch experiments. In this case, the 20mL mixture was agitated at 40 rpm until equilibrium was reached. To establish the equilibrium time, tubes containing a 1 mg.L^{-1} solution of PPCPs and 10 mg of cork were agitated and a maximum of four samples of 0.5mL each were periodically taken from the 20 mL mixture and then analysed by HPLC-DAD using the method that has been described in section 3.2. The samples were filtrated with 0.2 μm nylon syringe filters before injection (Sigma Aldrich, Germany).

Figure 3.6. a) Granular cork and cork stopper and plate, b) experimental set-up for batch desorption experiments.

4. RESULTS AND DISCUSSION



4.1 State of knowledge regarding microextraction techniques in the determination of pharmaceutical and cosmetic products in environmental water samples.



4.1.1 Precedents

Pharmaceutical and personal care products (PPCPs) are classified as emerging contaminants as they are regarded as possible threats to the aquatic environment and human health [197, 198]. Given that these contaminants are not target compounds of industrial and sewage treatment plants, they are normally not eliminated and therefore are able to make their way into sources of drinking water such as river waters and lakes [199, 200]. The organic compounds mentioned in this review are Pharmaceuticals, including non-steroidal anti-inflammatory drugs such as ketoprofen (KTP) and naproxen (NAP), antiepileptics, such as carbamazepine (CBZ), and analgesics, such as sodium diclofenac (DCF), and ingredient of personal care products, including antiseptic, such as triclosan (TCS).

In order to assess the quality of surface water, it is essential to develop sensitive, reliable and rapid methods to detect PPCPs. Most of our current understanding of the fate, transport, and effects of environmental PPCPs stems from grab sampling of water, brought back to the laboratory for extraction and concentration into a form that is suitable for instrumental analysis, typically several methods for analyzing NSAIDs in surface water are based on a highly efficient enrichment and separation method coupled with a sensitive detection technique such as gas chromatography (GC) or liquid chromatography (LC), particularly coupled to mass spectrometry (MS) and tandem mass spectrometry (MS/ MS) [201].

Several extraction and preconcentration techniques have been developed for the determination of organic compounds at trace levels in environmental waters. The main purpose of sample preparation is to eliminate interfering compounds and to increase the sensitivity of the method by preconcentrating the sample. Ideally the sample preparation technique should be simple, fast, selective, inexpensive and suitable for miniaturization [101]. Conventional sample preparation techniques are liquid-liquid extraction (LLE) and solid-phase extraction (SPE) described in the introduction chapter, but these techniques have the drawbacks of being time-consuming and requiring large amounts of organic solvent. To overcome these issues, in the last decade attention has focused on the development of miniaturized extraction techniques such as solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE) and liquid phase microextraction (LPME) which are easy techniques to use, require low organic solvent consumption and do not require multistage operations. In this section, we review the most popular sorptive microextraction techniques, such as, SPME, SBSE, and silicone rods although novel sorptive extraction techniques that have recently emerged are also discussed

and their applications toward the determination of PPCPs in environmental liquid samples using LC-MS/MS, GC/MS and HPLC-DAD.

4.1.2. Solid-phase microextraction (SPME)

Solid-phase microextraction (SPME), first developed in the early 1990s by Arthur and Pawliszyn [102], as a solvent-free, miniaturized technique that could be used as a green alternative to conventional techniques [102]. SPME has been used to extract analytes from gaseous, liquid, and solid matrices and allows sample collection, extraction, analyte enrichment and isolation from sample matrices to be integrated in a single procedure. SPME technology is a non-exhaustive technique based on the partition equilibrium of analytes between the sample matrix and the extraction phase [101]. SPME techniques can be classified roughly into static in-vessel and dynamic in-flow microextraction. Static procedures, which include fibre SPME, thin-film microextraction (TFME), in-tube SPME, rotating disk sorptive extraction (RDSE), stir bar sorptive extraction (SBSE) and dispersive SPME, are typically carried out in stirred samples (Figure 4.1)

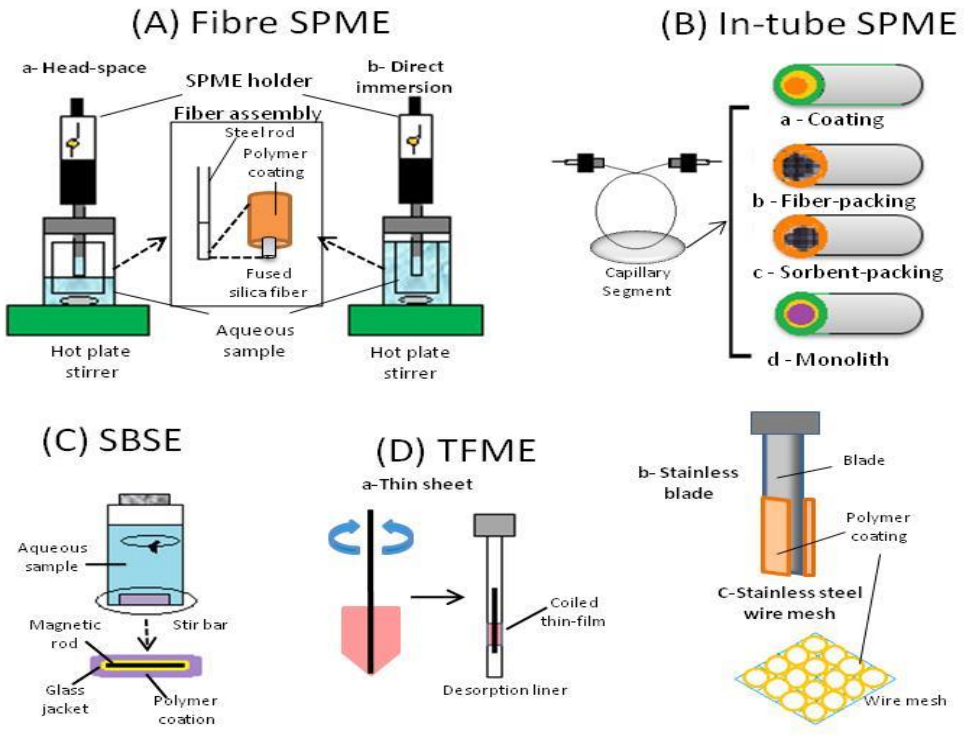


Figure 4.1. SPME devices and related microextraction techniques [101].

Fibre SPME, which uses a sorbent coating on the outer surface of a fused silica fibre to extract the analyte(s) from the sample matrix, is the most common format (Figure 4.1A).

Depending on the position of the fibre in relation to the sample, microextraction can be performed in two modes [202]; direct immersion (DI) in which the fibre is immersed in the sample, and adsorption from the headspace (HS) in which the analytes are first transferred from the sample to the gas phase [203]. This latter mode is particularly appropriate for volatile and semi-volatile species, whereas the former extraction mode can be used independently of the volatility of the analyte.

The desorption of the analytes from the coating can be carried out either thermally by direct insertion of the fibre into the GC injector using an appropriate solvent or by coupling to LC with a specific device. In the case of GC analysis, the thermal desorption (TD) of analytes from the coated fibre is one of the main reasons for the broad applicability of this coupling (SPME-GC) [204].

There are several parameters to optimize in the SPME technique that affect the equilibrium constant and equilibration time. These include fibre type, thickness of the stationary phase, fibre length, extraction mode, sample volume, time and temperature of extraction, and salting out [205]. Once the fibre has been exposed to the sample matrix, the transport of analytes from the matrix to the coating material takes place immediately. Extraction is complete when distribution equilibrium between the sample matrix and coating material is achieved. There are several commercial coated SPME fibers available in varying thicknesses and with single coatings, including polydimethylsiloxane (PDMS), divinylbenzene (DVB), carboxen (CAR), polyethylene glycol (PEG), polyacrylate (PA) and carbowax (CW) and mixtures of copolymers such as PDMS/DVB, PDMS/CAR, and CW/DVB [101, 202, 206]. Some of them have been used for the extraction of PPCPs in environmental water samples [204, 207, 208]. One of the limitations of SPME is the determination of polar organic contaminants, but this may be solved with a derivatization step. Derivatization can increase the volatility and reduced the polarity of the same analytes and can therefore improve the extraction recovery, selectivity and detection of the analytes. Derivatization can be performed in different modes: direct derivatization, derivatization on the SPME fibre and derivatization in the GC injection port. Derivatization on the SPME fibre was used in the development of an HS-SPME method for the determination of anti-inflammatories, oestrogens, antiseptics and bisphenol A by GC-MS [208].

Table 4.1 summarizes some applications of different SPME coatings for the determination of PPCPs in a variety of sample matrices.

Another format of SPME for sample preparation is in-tube SPME also called capillary microextraction (CME), which consists of an open tubular fused-silica capillary with an inner surface coating or a sorbent bed, thereby overcoming fibre related drawbacks such as fragility, low sorption capacity and bleeding from thick-film coatings [101]. The SPME device was developed for coupling with chromatographic techniques and it can either be placed between the autosampler injection needle and the loop or attached in the position of the autosampler injection loop. In this device, analytes in aqueous matrices are directly extracted and concentrated by the coating in the capillary column through repeated with drawal and expulsion of the sample solution, before being directly transferred to the GC or LC instrument. Automation via coupling of the SPME device to an autosampler allows all the steps of SPME (sample incubation, temperature control, fibre cleaning, extraction time and desorption time) to be conducted by an integrated computer-operated system [209, 210]**.**

The coatings used in this format are similar to commercially available SPME fibres. The literature also makes reference to coatings tailored for specific compounds, including molecularly imprinted polymers (MIP) [211, 212], and ionic liquids. The high viscosity of the ionic liquids improves the quality of the fibre coating and, at the same time, the use of the appropriate cation-anion pair can result in high selectivity of the extraction process [213, 214]. The use of polymeric ionic liquid coatings for SPME made it possible to quantitatively extract pharmaceutical compounds such as KTP (94.8%) and sodium DCF (95.3%) (see Table 4.1) [215].

However, MIPs have been applied in the selective analysis of a single NSAID, such as ibuprofen or diclofenac [216, 217] and multi template MIPs in the determination of ketoprofen and other NSAIDs in wastewaters [218]. Higher extraction recoveries ranging between 68% and 114% have been obtained by Silindile et *al.* [219] when a synthesized MIP material for an SPME device was applied to the determination of KET in aqueous samples as can be seen Table 4.1. On the other hand**,** PDMS SPME fiber demonstrated good performance in terms of recovery of TCS using HPLC-DAD (99% to 100%) [220].

The main advantages of SPME are that it eliminates the need for solvents and it is fast, simple and sensitive. Furthermore, it permits the determination of polar and non-polar analytes in a wide range of matrices. The disadvantages are the possibility of batch-to-batch variation of the fibre coatings, the occasional lack of robustness of these coatings and the limited range of the stationary phases [221].

Table 4.1. Application of different SPME coatings for the determination of PPCPs in environmental water samples.

Analytes	SPME fiber	Matrix	Instrument	Recovery (%)	LOD ($ng.L^{-1}$)	Ref.
KET	PDMS/DVB-PA	River water	GC/MS	105.1	0.1	[222]
NAP				96.4	0.12	
NAP	PDMS	Tap water	GC–MS	100	2.7	[223]
		River water		102.7		
CBZ	PDMS–DVB	River water	LC–DAD	71.6- 122.8	3	[224]
DCF					1.5	
NAP					0.5	
KET					2.2	
CBZ	PDMS–DVB	River water	LC–DAD	72- 125	-	[225]
DCF						
NAP		Wastewater		83-140		
KET						
KET	MIP	Wastewater	HPLC	68	230 (influent)	[219]
					170 (effluent)	
KET	PIL	Lake water	HPLC	94.8	200	[215]
DCF				95.3		

Table 4.1. Application of different SPME coatings for the determination of PPCPs in environmental water samples. (Continued)

Analytes	SPME fiber	Matrix	Instrument	Recovery (%)	LOD ($ng.L^{-1}$)	Ref.
TCS	DVB/ CAR/PDMS	River water, wastewaters, swimming pool water	GC-MS/MS	87-101	6.5	[226]
TCS	PDMS	River water	HPLC-DAD	99-110	470.0	[220]
			HPLC-MS/MS	99-110	1.37	

4.1.3. Stir bar sorptive extraction (SBSE)

SBSE, introduced in 1999 by Baltussen et al. [103], is used for the extraction and enrichment of target analytes from aqueous solutions. The extraction process is based on the partitioning equilibrium of target analytes between the coating on the stir bar and the sample matrix, whose fundamentals are similar to SPME. The main difference between these two techniques is that in SBSE the amount of sorptive phase is 50 to 250 times higher than SPME, giving the former greater capacity, hence, permitting higher absolute recoveries to be achieved [227].

During the extraction, the analytes are retained onto the coating depending on the sample pH, the agitation speed and the ionic strength, among other factors.

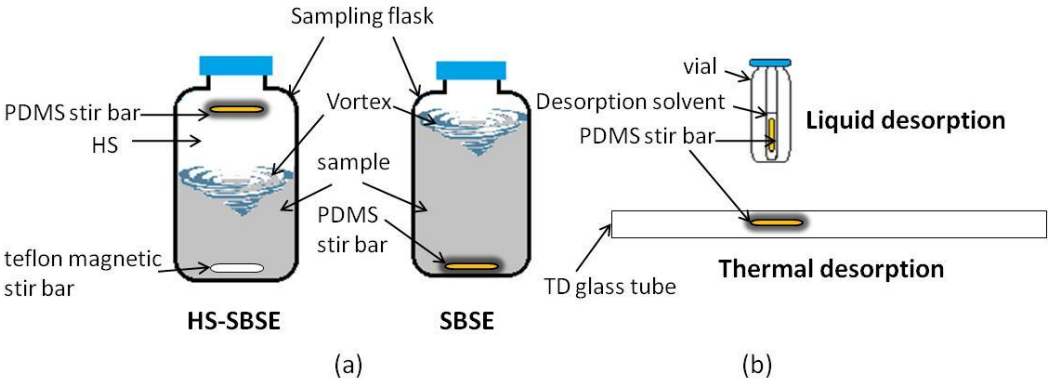


Figure 4.2. (a) SBSE sampling modes, (b) SBSE desorption [228].

Figure 4.2 shows a schematic diagram of the extraction and desorption of the SBSE technique that can be applied in different extraction modes: immersion and headspace (HS) and, in the case of desorption, by liquid (LD) or thermally (TD) [229-231]. When SBSE is combined with gas chromatography (GC), TD is the most common technique since the stir bar is introduced into a TD unit and the analytes are directly desorbed to the column for further analysis. Although TD provides high sensitivity, it requires the use of a TD unit which is often not available in standard laboratories. LD has been widely applied for the determination of labile and polar compounds followed by liquid chromatography (LC). LD is performed by the immersion of the stir bar in a small volume of an organic solvent. Thus, the choice of the organic solvent, its volume and desorption time are important factors to bear in mind during SBSE optimization [232, 233].

Recent SBSE-related reviews have mainly focused on its application in environmental, food and biological analysis [229, 231, 232, 234, 235]. Polydimethylsiloxane (PDMS) is the commercial available coating that is most widely used in SBSE. This polymer is able to extract pharmaceuticals [135, 236], personal care products (PCPs) [237-240] and pesticides [241, 242], that have apolar and semi polar characteristics from different matrices. Therefore, the challenge in SBSE has been to develop polar coatings to increase the versatility of SBSE. Two new polar coatings for SBSE have been registered by Gerstel. One of these known as Acrylate Twister® is based on polyacrylate (PA) and the other known as EG Silicone Twister®, in a poly (ethylene) glycol (PEG) modified silicone. These new commercial polar coatings for SBSE have been evaluated and compared with the PDMS coating for the extraction of a wide range of PPCPs from wastewater samples, showing that EG Silicone has better performance in terms of recovery for the less polar compounds (40% to 80%) [243]. Ramirez et *al.*[240] developed an SBSE/(TD) method to determine PPCPs by GC-MS in different water samples**.** In this study, the extraction and derivatization steps were carried out at the same time and the different parameters affecting both SBSE extraction and TD were optimized. EG Silicone Twister has been applied to the determination of bisphenols by GC–MS [244]. In this method, TD was used and did not require the derivatization step that is generally required when PDMS coating is used. More recently, Tanwar et *al.* [245] also developed an SBSE/LD/LC-MS/MS method for the determination of NSAIDs in water samples using a commercial EG-silicone coating. In these studies, the authors compared the efficiency of both, EG-silicone and PDMS, coated SBSE, bars for extracting NSAIDs, showing that EG-silicone provide the highest recoveries (Table 4.2).

Commercially available polar coating materials give poor results or are completely ineffective in the case of many polar compounds of interest and so efforts are being made to develop novel SBSE coatings that enhance extraction from complex matrices. Different technologies can be used to synthesize in-house coatings that are able to retain polar compounds and provide thermal and mechanical stability.

One of these technologies is sol–gel, which allows the preparation of solvent resistant, thermally stable thick films that provide good repeatability and a long lifetime, due to the chemical bonding between the surface of the glass and the coating [229]. A hybrid sol-gel derived coating combining cyanopropyltriethoxysilane (CNPrTEOS) and PDMS was developed by Ibrahim *et al.* to extract both DCF and KET from water samples [246]. Monolithic materials are another approach in the preparation of SBSE coatings which are

particurly attractive due to their simplicity: a monomer mixture with a porogen solvent is polymerized to form a porous polymer containing a network of interconnected pores of low micrometer sizes. The advantages of monolithic materials are high permeability, favourable mass transfer and low cost [229]. Monolithic materials can extract both non-polar and polar compounds effectively. Several monomer mixtures have been studied to extract PPCPs from water samples [143, 144, 247]. Two new coatings, which can extract emerging pollutants with a wide range of polarities, were prepared with either 2-hydroxyethyl methacrylates (HEMA) and DVB in the case of poly(HEMA-co-DVB) or polyethylene glycol monoethylacrylate (PEGMA) and pentraerythritoltriacrylate (PETRA), as the cross-linker, in the case of poly(PEGMAco-PETRA) [248]. The monolithic SBSE coating, which is able to extract polar PPCPs from wastewater samples, contained a great number of ester and hydroxyl groups [144].

Molecularly-imprinted polymers (MIPs) are another type of selective coating for SBSE. These have shown great selectivity and rapid adsorption equilibrium in the case of highly specific systems [212].

Despite the development of new polymeric phases for the more polar compounds, PDMS is still the most widely used coating for SBSE due to its stability, reusability and robustness.

Table 4.2. SBSE-based methods for the determination of PPCPs in environmental water samples.

Analytes	Matrix	SBSE-coating material	Separation and detection techniques	Optimal parameters of extraction and desorption	Recovery (%)	LOD ($\mu g.L^{-1}$)	Ref.
NAP	Ground, river and wastewater	PDMS	LD/GC–MS/MS	500 rpm, 15 mL, pH 2, 5 g NaCl, 240 min, des. 200 µL of ethyl acetate	70 to 130	0.019	[249]
KET						0.013	
DCF						0.021	
CBZ						0.088	
TCS						0.029	
NAP	Sea, River water, wastewater	PDMS	LD/HPLC-DAD	PDMS 1000 rpm, 25 mL, pH 2, 4 h des. 1.5 mL ACN, 30 min	9.8	1.0	[135]
		PU			78.3	0.4	
DCF		PDMS		PU 1250 rpm, 25 mL, pH 2, 6 h des. 5 mL ACN, 15 min	34.6	1.6	
		PU			77.7	0.7	
DCF	Liquid formulation	PDMS	HPLC–UV	600 rpm, 25 mL, pH 2.5, 120 min des. 5 ml ACN, 40 min	70	16.06	[250]
CBZ	Wastewater	PDMS, PA and EG Silicone	LD/LC–MS/MS	1000 rpm, 50 mL, pH 5, 4 h, des. 1 mL MeOH, 15 min (PA:60 min)	<1	0.0025 to 0.1	[243]
DCF					<1		
TCS		PDMS			40		
		PA			42		
		EG Silicone			80		

Table 4.2. SBSE-based methods for the determination of PPCPs in environmental water samples. (Continued)

Analytes	Matrix	SBSE-coating material	Separation and detection techniques	Optimal parameters of extraction and desorption	Recovery (%)	LOD ($\mu g.L^{-1}$)	Ref.
KET **NAP** **DCF**	river and tap water	EG-Silicone, PDMS	LD/LC–MS/MS	500 rpm, 40 mL, pH 2, 3 h, des. 800 µL ACN, 40 min.	-	0.06 0.071 0.0111	[245]
CBZ **DCF**	River water, effluent and influent waste water	Hydrophilic polymer based on poly(N-vinylpyrrolidoneco-divinylbenzene)	LD/LC–MS/MS	900 rpm, 50 mL, pH 5, 4 h des. 5 ml MeOH, 15 min	83 80	0.01 to 0.020	[247]
NAP **DCF** **CBZ**	Environmental water	poly(MAA-co-DVB) methacrylic acid	LD/LC–MS/MS	750 rpm, 100 ml, pH 3, 4 h des. 5 mL MeOH, 20 min	107 101 95	0.05 0.01 0.01	[143]
TCS	River water	PDMS	LD/GC-MS	900 rpm, 100 mL,10 h, des. 2 mL ACN, 30 min	65	0.005	[251]

4.1.4. Silicone rods (SRs) extraction and silicone tubes (STs) extraction

Technical silicone sorbents such as silicone rods (SRs) and silicone tubes (ST), made of a polymeric material, are a low cost alternative to SBSE that was first introduced by Popp et al. in 2004 for the enrichment of organic compounds [252, 253]. Similar to the above mentioned sorptive extraction techniques (SPME and SBSE); the SRs technique is also based on the partitioning of the analytes between the aqueous or gaseous phase and the polymeric phase. The interactions of the analytes with the polymeric material are much weaker compared to active surfaces resulting in analyte desorption to be performed under softer conditions avoiding analyte degradation.

The commercially available rods are made with polydimethylsiloxane (PDMS) but most of them are silicone or polysiloxane materials consisting of PDMS with some additives such as silicic acid esters are added as fillers [254]. For example, the STs provided by Reichelt Chemietechnik GmbH (Heidelberg, Germany) consist to only 70% of PDMS [255].

In the laboratory the flexible silicone elastomer tube is cut in small pieces (i.e. 1-2 cm long) and weighted to ensure that each time the same volume is used. These pieces are cleaned and conditioning with a solvent or heated for a few hours at 250ºC under a nitrogen stream. Generally, the SR is put into the liquid sample and shaken until equilibrium is achieved. The extraction times depend on the sample and silicone rod volumes, the physico-chemical characteristics of the analytes and the pH, salinity and type of the sample. After extraction, the SR is removed from the sample and liquid desorption (LD) with HPLC analysis [252] or thermal desorption (TD) prior GC analysis [252] can be performed. However as, in some cases, TD may cause noisy chromatographic backgrounds due to the degradation of the SR material, LD with a small volume of an organic solvent is, in general, used as alternative [256]. The different steps involved in SR extraction are presented in Figure 4.3. The extraction times to reach equilibrium are very different and depend on the applied sample and silicone volume as well as on the physical and chemical properties of the analytes. It is possible to work under non-equilibrium conditions when all other parameters are kept constant.

Despite being a relatively new technique, Prieto et *al*. developed an LD/GC-MS/MS method for the determination of organic pollutants, including triclosan, in water samples using different bulk polymeric materials, such as polyethersulfone (PES), polypropylene (PP) and

Kevlar (Kv) [257]. In this study, PES and PP tubes and Kv multi-filament yarn were tested and compared to PDMS rods (Table 4.3). It has been demonstrated that porous polypropylene membranes can extract compounds with high K_{ow} such as organophosphate esters (OPs) and halogenated anisoles from water samples [258, 259]. Kv is a polyamide polymer that has excellent thermal and organic solvent stability. Jinno et *al.* [260] prepared different functionalized fibres, with a Kv core, for the extraction of phthalates from water samples. In their work, it was proved that the un-derivatised polymer was also able to extract target compounds. Thereafter, the non-functionalised polymer was applied to the determination of PAHs in water samples, which resulted in detection limits in the low $ng.L^{-1}$ range [261]. On the other hand, PES is a well-known polymeric material that shows outstanding oxidative, thermal, and hydrolytic stability as well as polar properties. Novel BPA-imprinted PES microspheres were applied in the determination of bisphenol A (BPA) in wine samples [262] and PES-based membranes in microdialysis applications [263, 264].

Silicon sorbents, such as silicon rods (SRs), were introduced as a low-cost alternative to stir bars for the extraction of polycyclic aromatic hydrocarbons [252] and polychlorinated biphenyl compounds [253]. Since then, SR extraction has mainly been applied to the extraction of chlorophenols [265], chlorobenzenes [255], phenolic compounds [266], pesticides [267], sixteen halogenated flame retardants, pharmaceuticals [268] such as carbamazepine, diclofenac, naproxen [135, 142, 269], and the ingredients of personal care products, such as triclosan [139].

Although SRs are robust and easy to manage, the higher amount of the acceptor phase PDMS in SBSE and SPME results in greater extraction efficiency, very high sensitivity at the sub-ppt level and good reproducibility. Despite the benefits of these techniques, the fact that they are patented technologies makes them particularly costly and so it is import for new low-cost sorbent materials to be developed. In this respect, technical silicone sorbents such as silicone tubes (STs) or silicone rods are particularly useful. The main advantage of the STs and SRs is that their low cost (ca. 5 cents a piece) makes them disposable [270]. Therefore they can be discarded after a single use, eliminating carry-over problems. Moreover, the extraction material can easily be adjusted to specific needs of an extraction task, by varying the length and thickness of the rods and tubes to address different sample volumes and analyte concentrations. Therefore the applications range is hardly limited because SRs and STs are

available in numerous lengths, thicknesses and with different diameters [270]. Further potential of SR and ST extraction lies in their application for in situ derivatisation or post extraction derivatisation techniques. An *in situ* derivatization method based on polydimethylsiloxane rod extraction followed by liquid desorption and chromatographic analysis by HPLC-DAD was developed for the determination of phenolic endocrine disrupting compounds such as bisphenol A, trichlorophenol, pentachlorophenol,4-nonylphenol, and 4-octylphenol in water samples [266].

Van Pinxteren et *al.* published a good review of the applications of PDMS rods and PDMS tubes for sample preparation [255]. The ultimate goal of these devices is to increase the sensitivity of the analytical method by improving the extraction efficiencies by increasing the PDMS volume. SRs and STs of different sizes and volumes of silicone (8–635µL) have so far been applied for the extraction/preconcentration of a large variety of organic micropollutants from different matrices. Moreover, SRs and STs can easily be adjusted to specific needs of analytical requirements enabling their use in different applications, such as, as sorptive materials for passive sampling purposes [270]. In passive sample devices, the silicone-based sorbent is usually enclosed in a cellulose or low density polyethylene membrane bag forming the so-called MESCO that can be applied for the passive sampling of air and for sampling organic micropollutants in surface water and groundwater [271]. Bare silicone materials in different forms as rods, tubes or sheets have also applied in passive sampling of surface waters. After sampling, the passive sampler is brought into the laboratory and desorption of the analytes is performed [255].

The main advantages of SRs is their low cost, robustness and great flexibility, which allows different extraction demands such as very small sample volumes to be addressed. SRs and STs of different sizes and volumes of silicone (8–635 µL) and in many different geometric forms, including thin films, tubes and rods coatings on a fiber have so far been applied for the extraction/preconcentration of a large variety of organic micropollutants from different matrices [272], Moreover, PDMS tubes can also be used both as partition and permeation sampling devices. In the latter case, the outer surface of the tubes is used for sampling, and the analytes permeating to the inside of the tube are stripped using a solvent or gas for further analysis [273, 274].

Table 4.3. Application of silicone rod to extract PPCPs from water samples

Analytes	Matrix	SR material	Extraction technique	Desorption and analysis	Optimal parameters for extraction and desorption	Recovery (%)	LOD ($\mu g.L^{-1}$)	Ref.
CBZ **DCF**	Wastewater	SR (PDMS)	Direct with SRs	Solvent-LC–MS/MS	2 cm, 600 rpm, 50 mL, pH 6.04, 34 days des. 300 µL MeOH, 10 min	-	16 14	[142]
TCS	Wastewater	PDMS, PES, PP, Kv	direct immersion or headspace sampling	LD/GC–MS/MS	PES (2 mg): 750 rpm, 75 mL, pH 5, 300 min des. 100 µL of ethyl acetate, 15 min	-	0.005 (PES tube)	[257]

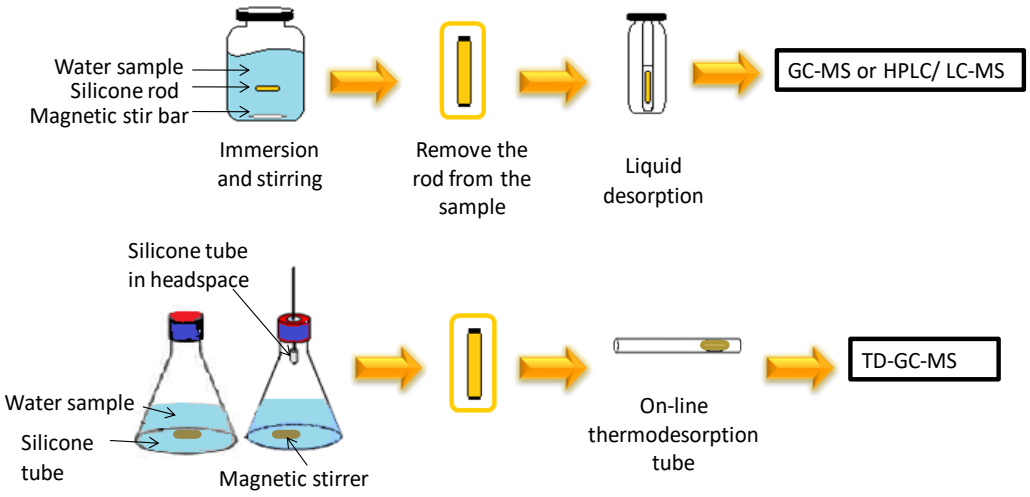


Figure 4.3. SR and ST extraction and desorption processes [255].

4.1.5. Other PPCP sorptive extraction techniques

In order to avoid the direct contact of the coating with the vessel when immersion sampling is performed with in-house SBSE coatings , new format such as rotating-disk sorptive extraction (RDSE), stir-rod sorptive extraction (SRSE), stir-cake sorptive extraction (SCSE), bar adsorptive microextraction (BAμE) or multi-sphere adsorptive microextraction (MSAμE)), Dynamic fabric phase sorptive extraction (DFPSE), fabric phase sorptive extraction (FPSE) have been developed that succeed in lengthening the lifetime of the coating material. To date, few studies have been published exploiting these new techniques. In this chapter we summarize their application in the extraction of PPCPs.

4.1.5.1. Rotating disk sorptive extraction (RDSE)

Rotating-disk-sorptive extraction (RDSE), proposed by Richter et *al.* in 2009 [275], uses a Teflon disk covered at the top with the stationary phase using the sol gel technique and has a magnetic stirrer placed underneath [276, 277]. This technique is useful for the extraction and preconcentration of low polarity analytes [276]. RDSE with polydimethylsiloxane (PDMS) as the sorbent phase has been used for the extraction and preconcentration of a series of emerging pollutants from water samples [275, 278-281].

In RDSE, the thin PDMS film has a higher surface-to-volume ratio, which enhances the surface contact with the sample, than SBSE (Figure 4.4A) at higher speeds (up to 1,600 rpm). The disk configuration can be easily made in the laboratory, and permits a larger exposed

surface area of the active phase to be immobilised. The overall extraction method is similar to that of SBSE [278]. After extraction, the disks, which can be reused several times, are dried and analytes desorbed with a small quantity of solvent [277, 281].

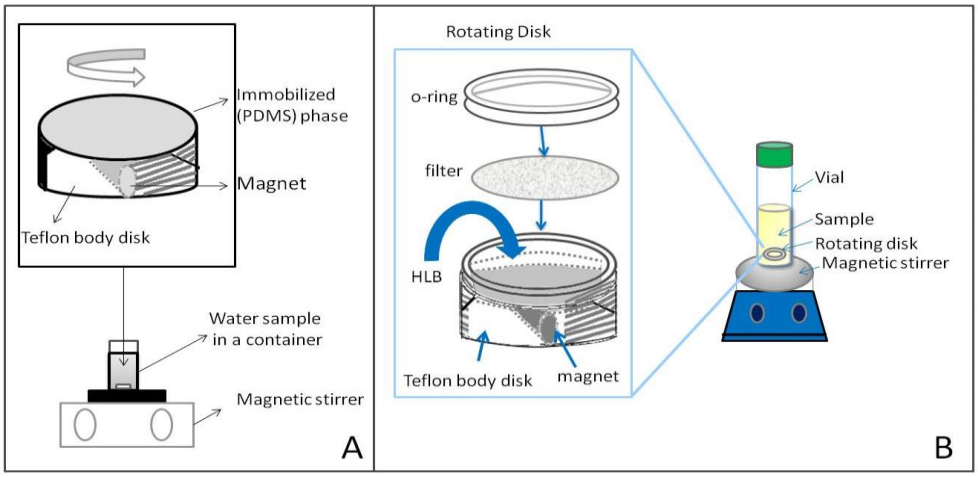


Figure 4.4. Schematic diagram of a rotating-disk-sorptive extraction device [282].

Manzo et *al.* have developed a proof-of-concept application of the RDSE system with C18 moieties as the sorptive phase as an LC front end and applied it in the determination of KTP, NAP and DCF in urine, giving high recoveries (101-102%) for KTP and NAP [277].

Following this general procedure, some polymeric SPE sorbents have been specially designed for the extraction of polar compounds. Richter et *al.* proposed a modification of RDSE which consisted of introducing a cavity into the unit that is loaded with polymeric sorbent (HLB) particles (Figure 4.4B) [283]. This cavity is covered with a filter to confine the particles, avoiding their loss during extraction. The great variety of commercially available SPE sorbents and their easy loading on the unit makes this approach highly versatile.

High selectivity and sensitivity in the determination of NSAIDs such as NAP, ibuprofen, KTP and DCF have been achieved using Oasis TM HLB as the sorbent phase in RDSE combined with UHPLC–UESI–TOF/MS analysis [284] or GC–MS providing successful recovery values for KTP and NAP [29] as can be seen in Table 4.4. RDSE gives higher recoveries of the target analytes than PDMS-based SBSE. Moreover, the versatility of the technique allows it to be coupled to different analytical instrumentation. When coupled with solid-phase spectrophotometry [279] a special PDMS coating needs to be synthesized to give high

transparency to the UV–visible radiation as the analytes are monitored directly on the surface of the coating.

RDSE, on the other hand, is, the most competitive solid phase approach as it minimizes the friction of the coating with the extraction vessel, permitting faster agitation [282]. However, RDSE has the disadvantages of requiring tight control of the extraction conditions and of being highly affected by the sample matrix [221].

Table 4.4. RDSE applications to extract PPCPs from different aqueous matrix samples.

Analytes	Matrix	RDSE material	Coupled analysis	Optimal parameters of extraction and desorption	Recovery (%)	LOD ($ng.L^{-1}$)	Ref.
NAP **DCF** **KET**	Wastewater	SPE-OasisTM HLB	UHPLC- UESI-TOF/MS[1]	3000 rpm, 25 mL, pH 2, 60 min, des. 5 mL MeOH 10 min at 2000 rpm x2 redissolved in 500 µL MeOH	98.6 95.1 107.8	3 8.9 2	[284]
KET **NAP** **DCF**	Wastewater	SPE-OasisTM HLB	GC–MS	3000 rpm, 50 mL, pH 2, 100 min, des. 5 mL MeOH 10 min at 2000 rpm x2, 500 µL of etthyl acetate derivatization with MTBSTFA	104 94 71	11 7 33	[29]
KET **NAP** **DCF**	Urine	Octadecyl C18-Silica gel	LC	1600 rpm, 20 mL, pH 2, 4 h. 1.2 mL MeOH.	101 102 106	35500 25300 21700	[277]

[1]**UHPLC-UESI**: ultra-high-performance liquid chromatography (UHPLC) coupled to an ultraspray electrospray ionization source (UESI) and time-of-flight mass spectrometry (TOF/MS).

4.1.5.2. Stir-rod sorptive extraction (SRSE)

Stir-rod-sorptive extraction (SRSE) was proposed by Luo et *al.* [285]. The device consists of a metal rod with a magnet in one of its ends. This end is covered by a glass insert to the surface of which a monolithic polymer coating is attached. The stir-rod device is introduced and fixed to the extraction vessel by a rubber plug which enables it to rotate in the sample at a stirring speed far below that used in SBSE (Figure 4.5). SRSE is used for the extraction and enrichment of analytes with different physical and chemical properties in complex environmental samples [285, 286].

Luo et *al.* [205] synthesized a polar monolith coating for SRSE by polimerisation of 4-Vinylpyridine (VP) and ethylene glycol dimethacrylate (EDMA) to be applied in the determination of NSAIDs in surface water and sewage by HPLC-UV, obtaining recovery values (>76%) without any deterotiation of the sorptive material to be observed after at least 60 experiments.

Although SRSE has a good extraction capacity, is easy to prepare, can be reused, has excellent longevity and there are many sorbents available for each type of application, the technique has strong matrix effects and tight control of extraction conditions is required. Further investigations is needed to develop this technique [221].

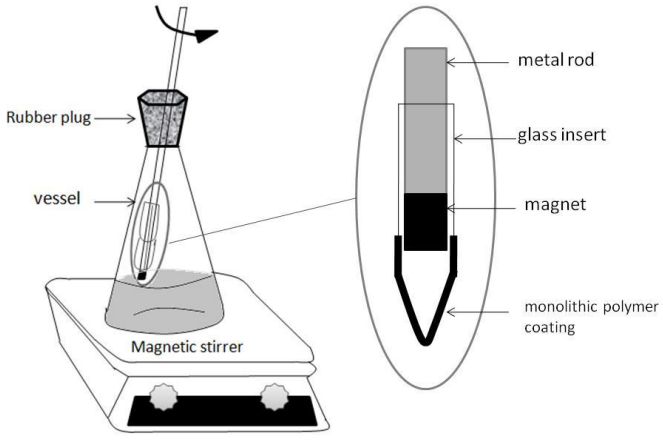


Figure 4.5. Schematic diagram of stir-rod-sorptive extraction [285].

4.1.5.3. Bar adsorptive microextraction (BAμE) and multi-sphere adsorptive microextraction (MSAμE)

Bar adsorptive microextraction (BAμE) is a novel static microextraction technique for trace analysis of polar compounds in aqueous media, introduced by Nogueira that uses nano-structured materials (e.g., activated carbons or polymers) for each particular type of target compounds [287]. This new analytical approach operates using floating sampling technology and it has shown high effectiveness in many applications, and also has the advantage over other sorption-based approaches (e.g. SBSE) that can be used for analytes with log K_{OW} < 3, even without derivatization steps or polymeric phases (e.g. polyurethanes) [288]. This technique takes advantage of the fact that polar solutes are easily adsorbed on specific solid materials with porous structures that have suitably active sites where the electrostatic and/or dispersive phenomena ("adsorption–desorption" properties) take place. These materials have large specific areas (≈1000 $m^2.g^{-1}$) that give remarkable adsorptive capacities (≈100–500 $g.mg^{-1}$) depending on the pH at the point of zero charge and texture. Different kinds of sorbent nanostructure allow the use of pH that are suitable for microcontaminants of a wide range of polarities. In practice, two geometrical variants are used: bar AμE (BAμE) and multi-sphere AμE (MSAμE) (Figure 4.6). The latter uses a sorbent in the form of a powder consisting of polystyrene-coated spheres, which are attached by a thread [269]. Different sorption materials can be selected to find which will provide the highest recovery factor (RF). Most of these materials, such as ACs, alumina, silica, polystyrene divinylbenzene (PS-DVB), modified pyrrolidone, alumina and silica-based polymers, are commercially available as they are also used as sorbents in SPE [228]. As well as the sorbents used, the analyte recovery depends strongly on parameters such as time of extraction and agitation speed and matrix characteristics such as pH, polarity and ionic strength [287].

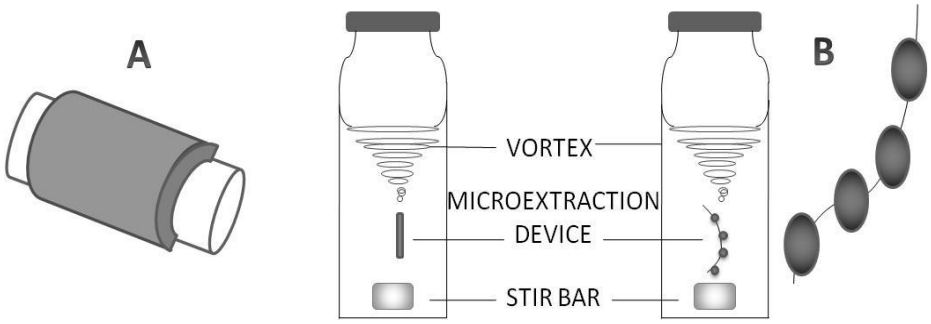


Figure 4.6. Micro extraction adsorption AμE devices: A) bar adsorptive microextraction and B) multi-spheres adsorptive extraction [289].

AμE techniques have been applied to extract and preconcentrate polar analytes (pesticides, pharmaceuticals and personal hygiene products and their metabolites from aqueous media and biological fluids [289]. The combination of BAμE with large-volume injection–gas chromatography–mass spectrometry resulted in low detection limits in the range 5-10 $ng.L^{-1}$ to be achieved and high recoveries for CBZ (> 80%) and TCS (> 75) [290].

BAμE with mixed sorbent phases (n-vinylpyrrolidone and divinylbenzene polymers with strong and weak anion exchangers), combined with liquid desorption followed by capillary electrophoresis with diode array detection ((PMIX)-LD/CE–DAD) allowed the determination of DCF and NAP in urine and water matrices [291]. The same extraction technique with N-vinylpyrrolidone polymer (NVP) as the sorbent, gave recoveries of 102.4; 87.4 and 74.5 % CBZ, DCF and TCS, respectively on environmental water matrices, including surface, sea, river and ground waters [137].

DCF, NAP and KTP were extracted by BAμE with P5 sorbent phase and the recoveries were compared with those obtained with five polymeric phases and five activated carbons. As can be seen in Table 4.5, P5 have proved to be the most effective sorbent.

Table 4.5. BAμE-based methods for the determination of PPCPs in environmental water samples.

Analytes	Matrix	Sorbent	Coupled analysis	Optimal parameters for extraction and desorption	Recovery (%)	LOD ($ng.L^{-1}$)	Ref.
DCF	Sea, river waters	N-vinylpyrrolidone polymer (NVP)	BAμE/μLD/HPLC-DAD	1000 rpm, 25 mL, 16 h, pH 5.5, des. 200μL of MeOH, 30min	87.4	20000	[137]
CBZ					102.4	20000	
TCS					74.5	30000	
TCS	Environmental waters	activated carbon (AC) polystyrene–divinylbenzene copolymer (PS-DVB)	BAμE/LD/GC-MS	1000 rpm, 25 mL, 16 h, pH 5, 5% NaCl for the AC phase des. 1.5 mL /MeOH (1:1), 45 min	73.6	10	[290]
CBZ					82.8	5	
TCS		(AC) (PS-DVB)				5	
CBZ						5	
KET	River, underground, estuary and sea waters, wastewater	P5 (0.9mg)	BAμE/μLD/HPLC-DAD	1000 rpm, 25 mL, 3 h, pH 5.5 des. 100 μL of MeOH, 30 min.	99.8	50	[136]
NAP					98.8	25	
DCF					99.3	100	
DCF	Sea, estuary and river waters	MAX/WAX	BAμE/PMIX-LD/CE–DAD	1000 rpm, 25 mL, pH 5.5, 16 h des. 200 μl MeOH/ACN (1:1), 30 min	96.9	300	[291]
NAP					86.6	300	

4.1.5.4. Fabric and dynamic fabric phase sorptive extraction

Fabric phase sorptive extraction (FPSE) is a sorbent-based sorptive extraction technique introduced in 2014 by Kabir and Furton [292], which is similar to SPME and SBSE. This technique is based on the principle of solid-liquid equilibrium extraction and consists of a flexible fabric substrate surface coated with different sorbent by sol-gel technology, which increases the primary contact surface area available for extraction [293].

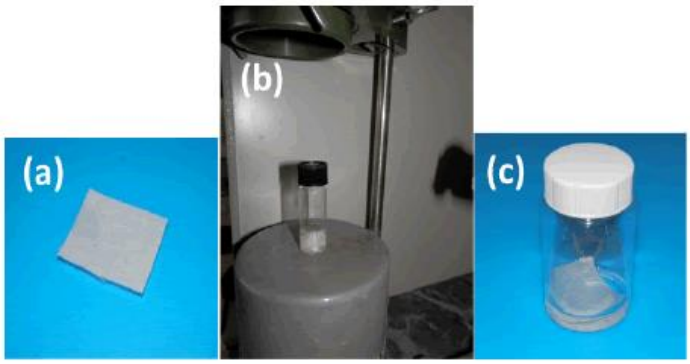


Figure 4.7. (a) FPSE device; (b) extraction with FPSE device; (c) solvent-mediated back extraction [294].

The amount of sorbent material use is an average 10 times greater than in SBSE. These sorbents have been developed to cover a wide range of analyte polarities and include: poly(dimethylsiloxane), poly(dimethyldiphenylsiloxane), poly(diphenylsiloxane), C18, C8, graphene, poly(tetrahydrofuran), poly(ethylenglycol), Carbowax 20M and poly(ethylene glycol)–block-poly(propylene glycol)– block-poly(ethylene glycol) [292]. The sorbent material is uniformly distributed on the cellulose / polyester / fibre glass fabric substrate. The solvent and chemical stability is high given that the amount of sorbent used is also high as well as the porosity. The sol-gel process allows the formation of a hybrid organic and inorganic polymeric network that anchors this network to the surface of the permeable substrate (cellulose/polyester/fibreglass) [295].

FPSE typically starts with the immersion of the device in a solvent to clean any unwanted residue, followed by rinsing with deionized water. An amount of sample containing the target analytes is placed in a screw-capped glass vial, and then the FPSE device is inserted into the

vial along with a clean magnetic stir bar. The sample solution is stirred for a defined extraction time until equilibrium is reached. The FPSE media is removed from the vial and the retained analytes are back-extracted with a small volume of an organic solvent. Finally, the eluent is centrifuged and filtered to remove any particulate matter prior to injection into HPLC or other systems [296]. Similarly to SPME and SBSE, the different variables affecting extraction and liquid desorption have to be evaluated for FPSE.

Table 4.6 summarizes the application of FPSE media in the extraction of pharmaceutical and cosmetic products.

Sameer et al. evaluated FPSE for the extraction of a group of PPCPs followed by liquid chromatography-tandem mass spectrometry (LC–MS/MS) with satisfactory results [297]. However, the main drawback of FPSE was the extraction time (4hours) required to reach equilibrium. The optimal conditions for the method were 50mL of sample and LD with 1mL of methanol for 5 min of stirring. Under these conditions, the recoveries were in the range of 20 to 92% for CBZ, 44% to 73% for DCF, 57% to 59% for TCS [297].

To overcome this long extraction time, a new FPSE approach, dynamic fabric phase sorptive extraction (DFPSE), has been proposed. DFPSE uses 47 mm circular disks of FPSE media coated with sorbent material of different polarities using sol–gel coating technology [293]. In the new FPSE extraction mode, the sample is percolated through the FPSE disks installed in a filtration apparatus. The retained analytes are then eluted by passing a small volume of the elution solvent through the same assembly. This configuration decreases the extraction time to 10min due to the large increase in the interfacial area.

The performance efficiency of the DFPSE technique was evaluated for the extraction of CBZ, DCF and TCS from river and wastewater samples, followed by LC-MS/MS analysis. Taking into account that CBZ is highly polar, a hydrophilic substrate such as cellulose would be a suitable choice. In addition, a polar polymer PEG was selected as the coating [295]. Recoveries were in the range of 18–53% for CBZ, 23–50 % for DCF, 22–43% for TCS.

Racamonde et al. have recently developed a method for the determination of NAP, KTP and DCF in environmental water samples by coupling FPSE with GC-MS. In this study, three different sol-gel coatings were evaluated: PDMDPS on a polyester substrate, PTHF and PEG on cellulose substrate [298]. PEG showed the best performance in terms of extraction recovery compared to the other two materials. Under optimal conditions, the absolute

recoveries were found to be between 93–111% for NAP, 92–108% for KTP, and 94–116% for DCF (Table 4.6).

FPSE have advantages such as small volumes of organic solvent for elution purposes, elimination of solvent evaporation, and a sample reconstitution step, make the technique environmentally friendly and cost effective in accordance with Green Analytical Chemistry requirements.

Table 4.6. Application of the FPSE techniques to extract PPCPs from water samples.

Analytes	Matrix	Fabric substrate	Sol-gel coating	Coupled analysis	Optimal parameters of extraction and desorption	R(%), Rapp (%)	LOD ($ng.L^{-1}$)	Ref.
CBZ	River water, Influent-Effluent wastewater	Cellulose	PEG	DPSE-LC-MS/M	50 mL, pH 3, 10% NaCl (w/v), 10 min des. 10 mL of ethyl acetate	18–53	4	[293]
DCF						23–50	2	
TCS						22–43	20	
CBZ	River water, Effluent-Influent wastewater	Cellulose	PEG	FPSE-LC-MS/MS	900 rpm, 50 mL, pH 3, 4 h des. 1 mL MeOH, 5 min.	20-92	10	[297]
DCF						44-73	1	
TCS						57-59	50	
NAP	River water, Wastewater	Cellulose	PEG	FPSE-GC-MS	500 rpm, 30 mL, pH 2, 120 min des. 1 mL ethyl acetate, 15 min.	93–111	2	[298]
KET						92–108	5	
DCF						94–116	2	

Rapp (%); Apparent recovery including the extraction recovery and the matrix effect.

4.1.6. Summary

The principles and innovations of sorbent-based microextraction techniques such as solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE), stir-rod-sorptive extraction (SRSE), bar adsorptive microextraction (BAμE), fabric phase sorptive extraction (FPSE) and silicone rod (SR)/silicone tube (ST) extraction have been revised with special emphasis on the determination of pharmaceuticals and ingredients of personal care products. The efforts made in the developments of these techniques to miniaturize the extraction devices, minimize the consumption of toxic and hazardous organic solvents, to eliminate sample pre-treatment and post-treatment steps, to reduce the sample volume, to reduce the extraction equilibrium time and to maximize the extraction efficiency etc. have been addressed. All these improved attributes are in accordance with the principles of green analytical chemistry. However, the main drawback of microextraction techniques is selectivity as most of the available sorbents have a limited capacity to extract highly polar compounds. This issue can be overcome by the introduction of new materials such as nanomaterials and MIPs as sorbents or by the use of in-house prepared sorbents. These innovative procedures also allow analytical performance to be improved by using well-known instrument configurations – such as HPLC-UV/Vis – while avoiding the use of more complex and expensive ones (HPLC-MS, UPLC-MS, etc.). Additionally, this instrumentation can also be used by non-expert operators in routine analyses both in clinical and quality-control procedures.

Furthermore, there is also a clear need for less costly and simpler microextraction techniques based on the use of bulk materials, such as silicone rods or silicone tubes. PDMS rod-based materials present similar efficiencies to those obtained by SBSE and meet analytical requirements in terms of purity, inertness and thermal stability. Other advantages of SRs are their greater flexibility and robustness, together with the fact that they can be discarded after a single use, eliminating problems of carry over. Moreover, PDMS tubes can also be used both as partition and permeation sampling devices.

4.2. Development of a silicone rod extraction based-method for the determination of NSAIDs and cosmetic products in water samples.

4.2.1. Precedents

Many analytical methodologies have been proposed to measure trace levels of organic micro-pollutants, including PPCPs, most of which are based on LC with DAD [2] or MS [200] detection. Trace level concentrations of PPCPs in environmental waters require the application of sample enrichment steps prior to their chromatographic analysis even if the most sensitive MS detection is used [290, 299, 300].

Various preconcentration techniques, such as solid-phase extraction (SPE) [301], solid-phase microextraction (SPME) [302] and liquid-phase microextraction (LPME) [303], have been developed to extract the PPCPs. However, SPE requires relatively large volumes of toxic solvents and is an expensive and laborious technique [301]. Although LPME is a simple technique that uses a small volume of organic solvent, it has some disadvantages, such as the long extraction time and, in the case of direct extraction, the limited number of suitable solvents. SPME does also not use large volumes of organic solvent, but it has disadvantages such as high cost, the fragility of the fibre and the need for a special device when combined with HPLC [303]. Other techniques have been developed that share the same sorptive principle as SPME but which are as simple to use as stir extraction. These include stir-bar sorptive extraction (SBSE), stir-rod-sorptive extraction, and stir-cake-sorptive extraction (SCSE) [221]. SBSE consists of a magnetic bar covered by a thin layer of a sorptive phase (e.g. polydimethylsiloxane (PDMS)) and provides improved extraction efficiencies in comparison with SPME given that SBSE uses a greater amount of PDMS, resulting in higher recoveries, greater sample capacity and sub-ppt level sensitivity [304]. On the other hand, SBSE has the drawbacks of being expensive and of having carryover effects, and the new coatings that are being developed have a limited capacity for reuse [305].

In recent years, Bar adsorptive microextraction (BAμE), that uses coatings of different sorbents, has been proposed for the extraction of medium-polar to polar compounds from aqueous media [305]. This technique has been applied in the determination of KET, NAP, DCF, carbamazepine (CBZ), and TCS [136, 137]. In the dynamic fabric phase sorptive extraction (DFPSE) technique, a flexible fabric substrate is coated using sol-gel technology with polymers containing different functional moieties to make them available for extraction and has been applied to the determination of CBZ from river and wastewater samples [293].

Other microextraction techniques, such as thin film PDMS and rotating disk sorptive extraction (RDSE), have been used in the extraction and preconcentration of various emerging pollutants from water samples [29]. RDSE consists of a rotating disk with a central cavity containing a sorbent phase that can extract NAP, ibuprofen, KET and DCF from water samples prior to their determination by UHPLC with time-of-flight mass spectrometry (TOF/MS) detection, allowing high sensitivities to be achieved [306].

Although all these techniques have great potential, less costly and simpler methods are required. Technical silicone sorbents such as silicone rods (SRs) area low cost alternative to SBSE that was first introduced by Popp et *al*. for the extraction of polycyclic aromatic hydrocarbons [252]. Silicone rod extraction has mainly been applied to the extraction of chlorobenzenes [307], priority organic pollutants [200] and halogenated-flame retardants [268] prior GC-MS analysis and for the determination of pharmaceuticals [142], phenolic compounds [266] and sunscreen compounds [254] by LC.
PDMS rod-based materials have the advantage over containing additives, such as vinyl methyl polysiloxane and silicic acid esters, which allow the extraction of medium-polar analytes. Other advantages of SRs are their greater flexibility and robustness, inertness, thermal stability and disposability, eliminating problems of carryover [255]. SRs can also easily be adjusted to meet specific analytical requirements enabling their use in different applications and as sorptive materials in passive sampling [267].

The main objective of this study is to develop a new analytical method for the determination of NAP, KET, CBZ, DCF, and TCS based on their extraction and preconcentration by PDMS rod. This step is followed by liquid desorption and high performance liquid chromatography (HPLC)-DAD analysis. The method was validated by analysing spiked surface water samples and applied to the determination of the target compounds in river waters. The analytical parameters of the developed method are compared with those obtained with other micro extraction-based techniques.

4.2.2. Study of PDMS rod extraction and desorption conditions for PPCPs

In order to find the best conditions of extraction and desorption for the preconcentration of the pharmaceutical and cosmetic products, a systematic study of several parameters was undertaken. In preliminary experiments, methanol proved to be the most efficient desorption solvent.

Kinetics of the extraction

Extraction time was evaluated by using an initial volume of 50 mL of a 100 μg.L^{-1} solution containing all the studied compounds. The pH of this solution was adjusted to 2 and 15% NaCl was added. Five different extraction periods (3, 5, 8, 10, and 24 h) were studied by analysing the remaining concentrations in the aqueous solution. As can be seen in Figure 4.8, equilibrium was reached at 10 h for all compounds.

The sorption efficiency for NAP, KET, CBZ, TCS and DCF are 19%, 17 %, 6%, 75% and 56%, respectively, showing that the PDMS has the highest affinity to compounds having log K_{ow} > 3 [229], as it is the case of TCS (log K_{ow} 4.7) and DCF (logK_{0W} 3.91). In the case of NAP, KET and CBZ, the efficiencies follow the same order than their hydrophobicities: CBZ (logK_{ow} 2.45) < NAP (logK_{ow} 3.12) < KET (logK_{OW} 3.1). It is known that in the case of PMDS sorbent the extraction efficiency, or recovery (R), correlates to the K_{ow} since the equation that describes the partition between the sorbent and the stationary phase is:

$$R = \frac{m_{SR}}{m_o} = \frac{K_{ow}/\beta}{1+(\frac{K_{ow}}{\beta})} \qquad (4.1)$$

where m_{SR} is the mass of analyte in the sorbent and m_0 is the mass of the analyte in the solution and β the ratio between the sample volume and the volume of the silicone phase [255]. High values of β in combination with lower or moderate partition coefficients led to a low recovery. The results obtained indicated that in the case of CBZ very low enrichment factors can be obtained using PDMS rod. However, all the subsequent experiments were performed with tall the target compounds.

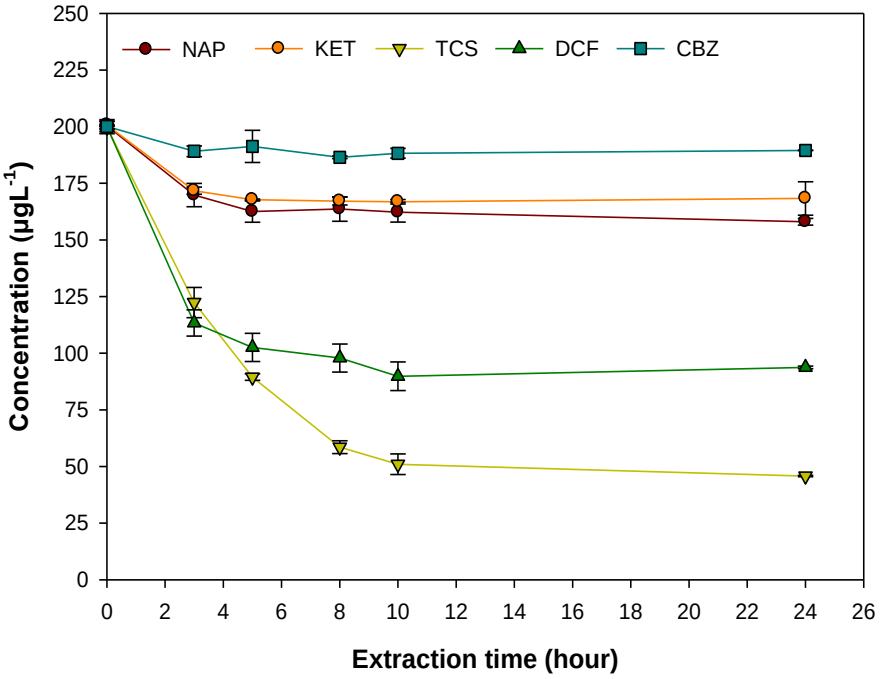


Figure 4.8. Kinetics of the extraction process (n=3). 50 mL of 200 µg.L^{-1} of PPCPs at pH 3, 15% NaCl.

4.2.3. Chemical conditions of the aqueous solution

4.2.3.1. Effect of pH

The effect of pH on the extraction efficiency was studied by immersing a 10 mm PDMS rod in 50 mL of ultrapure water containing 100 µg.L^{-1} of PPCPs for 10 h, as determined by the kinetic study. After equilibrium, the rod was exposed to 200 µL of methanol for 30 min. The sorption extraction of PPCPs by the PDMS rod strongly depended on the pH of the aqueous solution and hence the pH was adjusted with hydrochloric acid or ammonia solutions to different values (2.0, 3.0, and 6.0) as can be seen in Figure 4.9. The best results in terms of the concentrations of NAP, KET, DCF, CBZ, and TCS in the desorption solution were obtained at pH 2, especially in the case of TCS, the concentration of which increased significantly in comparison with pH 2. However, a slight decrease in the sorption of KET was obtained at pH 2. These compounds can be effectively adsorbed when they are present in their non-ionized form in the aqueous solution at pH < pK_a (DCF pK_a 4.3, NAP pK_a 4.15, KET pK_a 4.45, TCS pK_a 8.14 and CBZ pK_a 13.9). The pH of the solution was then adjusted to pH 3 in the subsequent experiments.

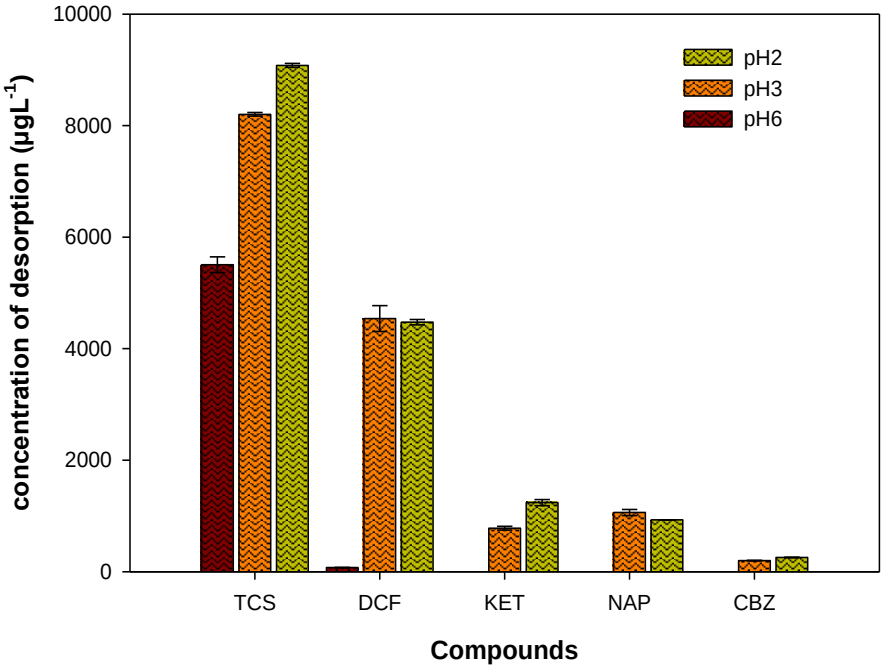


Figure 4.9. Effect of pH on the extraction of PPCPs (n=3). Initial: 50 mL of 100 µg.L^{-1} of PPCPs and 15% NaCl. Desorption volume: 200 µL and desorption time=30 min.

4.2.3.2. Effect of methanol addition

The addition of matrix modifiers such as methanol and NaCl to the aqueous solutions is a widely used practice in SBSE and SPME techniques. NaCl is added in order to cause a salting-out effect resulting in the improvement of the recoveries of polar analytes. However, there is controversy with regards to the addition of methanol, which is often added to the aqueous sample in order to reduce the adsorption of certain organic analytes on the glassware with the trade-off of increasing the solubility of the analyte in the donor phase [229, 268].
In this study, the addition of 5% methanol to the sample was investigated together with the desorption time (15 min, 30 min and 45 min). As can be seen in Figure 4.10, the desorption concentrations increased significantly without the addition of methanol at all time periods, although more significantly at 30 min, followed by 45 min, and finally 15 min. When 5% of methanol was added, increases in the desorption concentrations were also observed at 30min and 45min, although these were less than when no methanol was used (Figure 4.10).

The addition of methanol significantly decreases the desorption concentration of the PPCPs given that it also decreases the uptake of the target compounds by the silicone phase as the

presence of methanol favours the affinity for the liquid phase. Consequently, the method was performed without methanol.

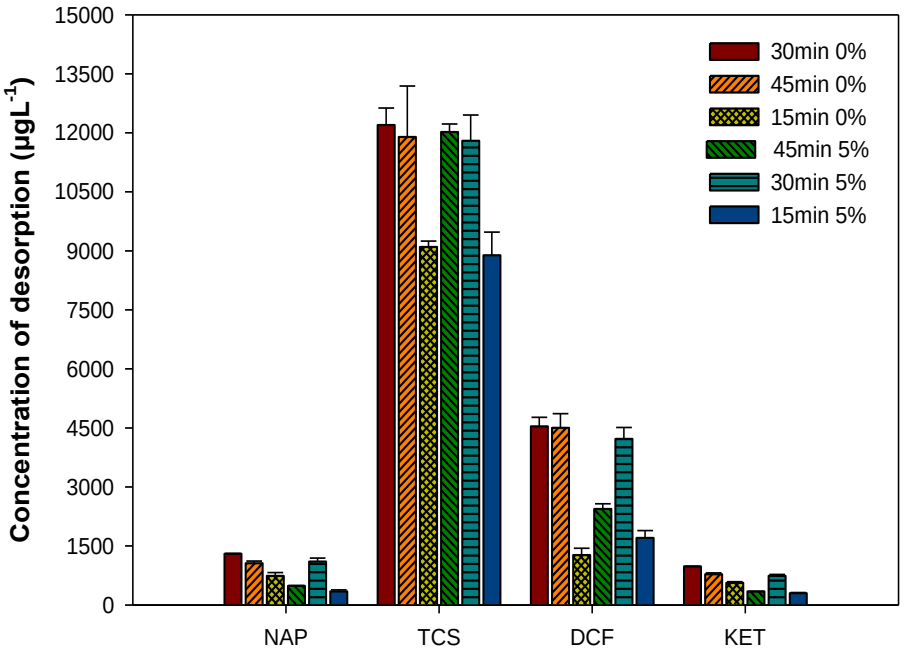


Figure 4.10. Effect of the addition of MeOH on the extraction of PPCPs (n=3) and of the desorption time. 50 mL of 100 µg.L^{-1} of PPCPs at pH 3 with the addition of 5% of MeOH and without modifier and 15% NaCl. Desorption volume of 200µL.

4.2.3.3. Effect of the ionic strength

As was stated above, the addition of an electrolyte may favour the migration of organic compounds from the bulk matrix to the sorbent ('salting-out' effect) [135, 229]. The main drawback of the use of NaCl as a modifier is that, in some cases, a decrease in the non-polar compound recoveries is observed as a result of a lower mass-transfer rate due to the increase in the water density. The effect of the ionic strength on the adsorption of the analytes was studied at four different concentrations of NaCl: 0, 5, 10 and 15% (w/v). As can be seen in Figure 4.11, the progressive addition of salt showed a significant increase in sorption efficiency, which is reflected in an increase in the desorption concentrations of TCS, NAP, KET, DCF and CBZ when the percentage of NaCl was increased to 15%. Thus, the addition of 15% NaCl to the aqueous solution was confirmed as the best conditions.

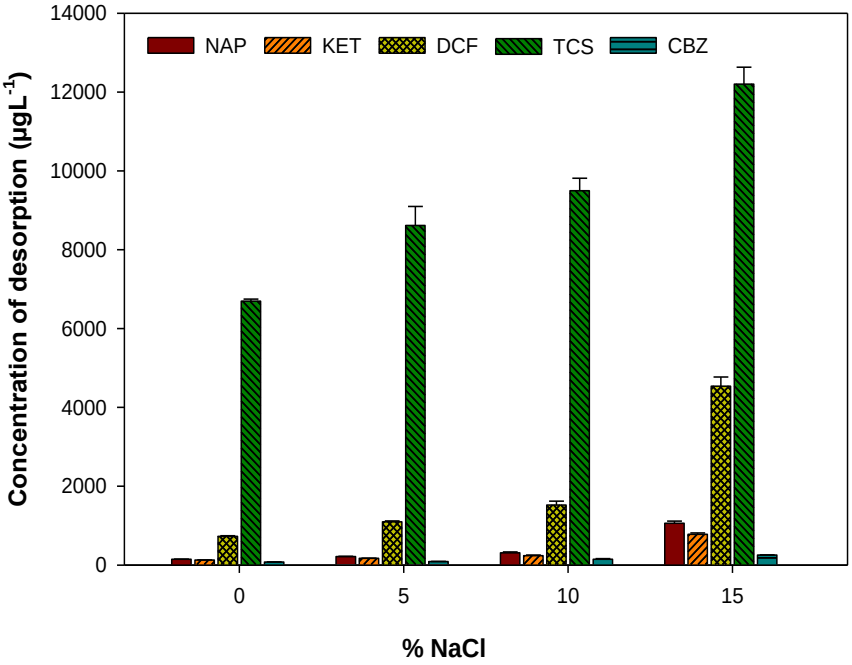


Figure 4.11. Effect of the addition of NaCl on the extraction of PPCPs (n=3). 50 mL of 100 µg.L^{-1} PPCPs solution at pH=3. Desorption volume: 200 µl and time of desorption: 30 min.

4.2.3.4. Effect of sample volume

Three different volumes 25, 50 and 100 mL, of ultrapure water samples containing 20 µg.L^{-1} of the target compounds were tested. NaCl at 15% was added to this solution and the analytes were extracted at 200 rpm for 10 h. Analyte desorption was again performed using 100 µL of methanol in an ultrasonic bath for 30 min The results of these experiments are presented as enrichment factors (EF), defined as the ratio of analyte concentration (C_{desor}) in the desorbed methanol solution and the initial concentration in the aqueous phase (C_0).

$$EF = \frac{C_{desor}}{C_0} \qquad (4.2)$$

The results obtained (Figure 4.12) showed that the EF for TCS increased significantly as the sample volume was raised to 100 mL whereas the increase in DCF was relatively slight. In the case of KET and NAP, the enrichment factor remained almost unchanged with 25 and 50 mL and decreases with 100 mL while for CBZ, the EF was only calculated with an initial volume

of 50 mL. Therefore, a 50 mL sample volume was selected for the following experiments in order to maximise the sensitivity of the method.

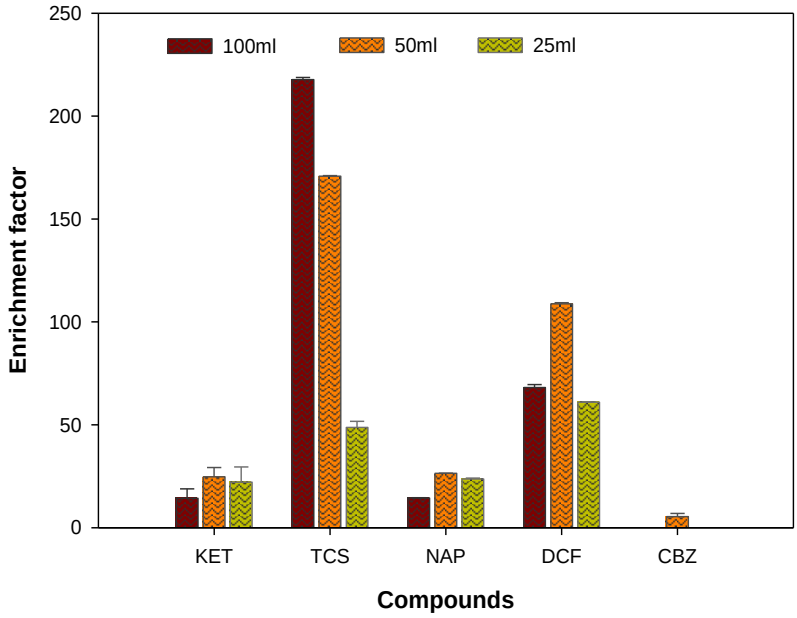


Figure 4.12. Enrichment factors obtained with different sample volumes (n=3). Initial concentration: 20 µg.L^{-1} of PPCPs at pH 2 and 15% NaCl. Desorption volume: 100 µL and desorption time of 30 min.

4.2.4. Desorption conditions

4.2.4.1. Desorption solvent

The back-extraction of the analytes from the silicone rod is a very important process to obtain high enrichment factors therefore, the desorption solvent must have sufficient capacity to strip the target compounds from the polymeric phase. Two desorption solvents, methanol and acetonitrile, were tested. Triplicate extractions were performed with ultrapure samples spiked at 100 µg.L^{-1} in the previously described conditions. After the extraction period, three consecutive desorptions of 30 min each, with 200 µL of solvent, sufficient to cover a 10 mm PDMS rod, were performed. However, some experiments were performed with 100 µL taking care that all the SR was immersed in the solvent.

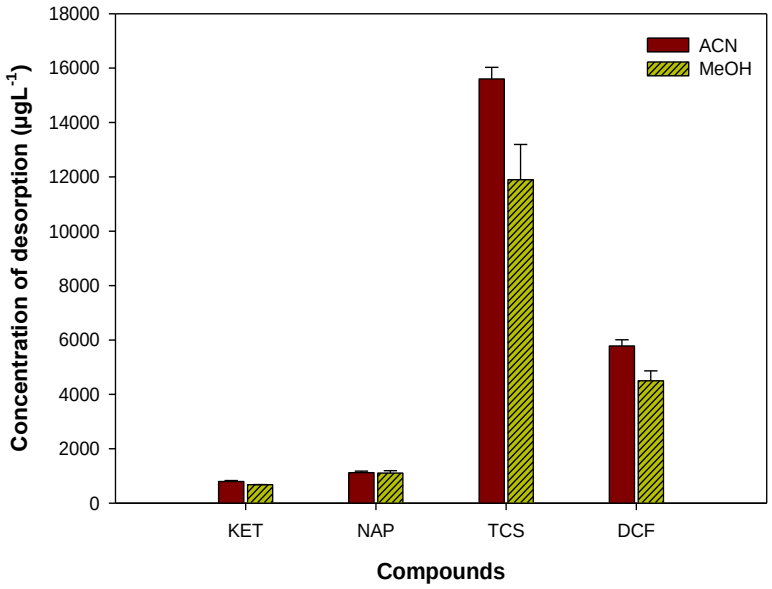


Figure 4.13. Effect of the desorption solvent on PPCP preconcentration (n=3). 50mL of 100 µg.L^{-1} PPCPs solution at pH 3 and 15% NaCl. Desorption volume: 200 µL and desorption time; 45min.

As can be seen in Figure 4.13, acetonitrile is slightly better than methanol in desorbing TCS and DCF, which are the most lipophilic compounds, and no differences were obtained between methanol and acetonitrile for KET and NAP. Hence, as good enrichment factors were obtained using both solvents, methanol was selected as the desorption solvent given that the use of this solvent facilitates the chromatographic analysis of the target compounds.

4.2.4.2. Desorption time and effect of the sonication in the desorption

After selecting the desorption solvent, back-extraction time was also evaluated at different periods (15, 30 and 45 min) as can be seen in Figure 4.14. In order to accelerate the stripping of the adsorbed compounds ultrasonic treatment was also tested, except in the case of 45 min, in which sonication was not used to avoid the risk of breaking the vial. The results obtained showed no significant difference between 30 min and 45 min desorption times with or without sonication for TCS, NAP, KET, whereas 15 min of sonication was only efficient in the case of DCF desorption. However, the efficiency was less than when 30 min and 45 min. were used. Sonication was not found to have a significant impact on desorption efficiency. Finally, a desorption time of 30 min without sonication was selected for its greater simplicity.

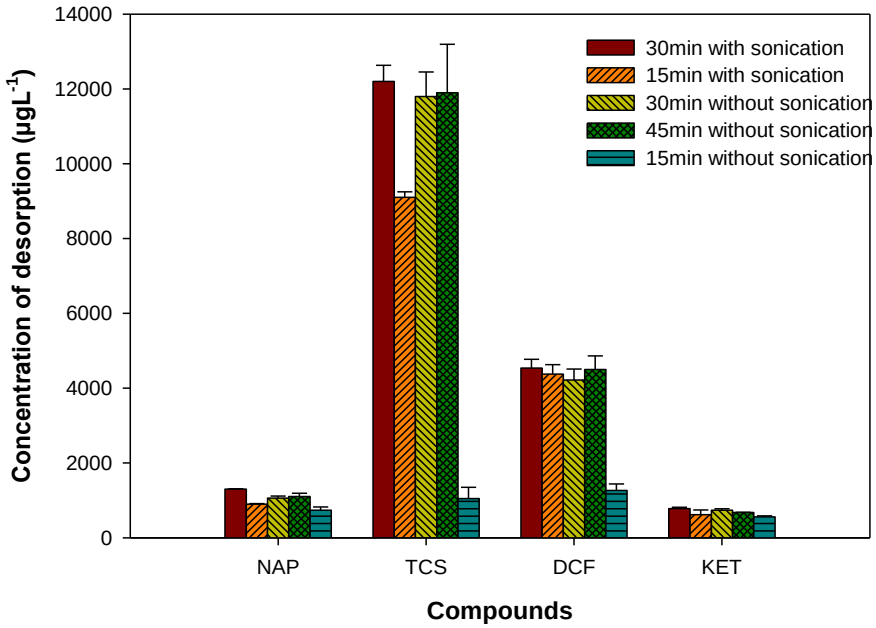


Figure 4.14. Effect of desorption time and sonication on the desorption of the extracted PPCPs (n=3). 50 mL of 100 µg.L^{-1} PPCP solution at pH=3 and 15% NaCl. Desorption volume: 200 µL.

4.2.5. Method validation

Linearity was evaluated by extracting triplicate ultrapure water samples spiked at five different concentration levels 10, 25, 50, 75 and 100 µg.L^{-1} of NAP, KET, CBZ, DCF, and TCS (Table 4.7). The concentrations were selected taking into account the different EF obtained for each compound as in the case of CBZ the EF is practically 1 and in the case of TCS, the most hydrophobic compound tested, the EF is 179. The method was linear for all compounds and determination coefficients (r^2) were higher than 0.990. The LODs and LOQs were calculated using the Excel regression analysis tool and considering a signal-to-noise ratio of 3 and 10, respectively. LODs ranged from 0.47 to 1.02 µg.L^{-1} except for CBZ, which was 3.40 µg.L^{-1}. LOQs ranged from 1.44 to 3.17 µg.L^{-1} except for CBZ, which was 10.33 µg.L^{-1}. The precision of the method, expressed as RSD%, was evaluated by replicate analysis (n = 6) of ultrapure water samples spiked at two concentration levels (25 and 100 µg.L^{-1}). Intraday precision was in the range of 0.4–9.7% at both levels and interday precision was between 3.8 and 10.5%, except for CBZ, which was 18.8%.

Table 4.7. Calibration curves, LODs, LOQs and precision of the developed method. The concentrations are in µg.L^{-1}.

Compounds	Retentin time (min)	Equations of calibration curve	Linearity (R^2)	RSD interday (%) (n=6) **25**	**100**	RSD intraday (%) (n=2) **25**	**100**	LOD (µg.L^{-1})	LOQ (µg.L^{-1})
KET	13.8	$y = 14.15x - 34.01$	0.999	3.8	4.7	0.4	6.0	1.02	3.17
TCS	17.5	$y = 96.5\,x - 76.68$	1	4.5	4.7	1.6	2.3	0.47	1.44
NAP	13.3	$y = 7.538\,x + 13.41$	0.999	10.2	10.5	0.5	0.4	0.56	1.70
DCF	15.5	$y = 38.62\,x + 88.79$	0.999	5.9	5.6	5.8	2.2	0.75	2.24
CBZ	11.12	$y = 2.094x - 54.82$	1	8	18.8	7.7	9.7	3.40	10.33

To evaluate the applicability of the present methodology to real samples, assays were performed by analysing spiked river water samples at concentrations of 10, 25, and 75 $\mu g.L^{-1}$ of NAP, KET, DCF, CBZ, and TCS. The recoveries obtained were in the 84.8–108.01% range at the lowest concentration level, 87.31–111.18% for the medium concentration level, and 86.53–103.98% for the highest concentration level, as can be seen in Table 4.9**.** Before performing the recovery experiments, the river water samples were analysed in order to ensure that the target compounds were not present and to characterise their main physico-chemical parameters (Table 4.8).

Table 4.8. Physico-chemical characteristics of the river water.

Quality parameters	**Units**	
Na^+	$mg.L^{-1}$	164.2
NH_4^+-N	$mg.L^{-1}$	0.2
K^+	$mg.L^{-1}$	16.8
Mg^{2+}	$mg.L^{-1}$	15.8
Cl^-	$mg.L^{-1}$	231.8
NO_2^--N	$mg.L^{-1}$	-
NO_3^--N	$mg.L^{-1}$	0.08
SO_4^{2-}	$mg.L^{-1}$	17.0
PO_4^{3-}	$mg.L^{-1}$	1.5
Ca^{2+}	$mg.L^{-1}$	65.8
COD	$mg.L^{-1}$	30
Conductivity	$\mu S.cm^{-1}$	1351

Table 4.9. Recoveries (%) of the target analytes by the developed methodology at three spiking levels.

Compounds	Concentration ($\mu g.L^{-1}$)		
	10	**25**	**75**
CBZ	-	-	99.07±1.59
KET	97.66±5.65	100.67±0.43	96.1±3.84
TCS	84.8±3.97	87.31±7.06	109.45±2.36
NAP	91.25±2.65	91.96±7.06	86.53±1.11
DCF	108.01±7.54	111.18±7.93	103.98±8.1

4.2.6. Comparison of the developed method with other microextraction-based methods

As can be observed in Table 4.10, the proposed methodology revealed better recovery levels for KET, NAP, DCF and TCS when compared with SBSE coated with polydimethylsiloxane (PDMS) [135, 139, 308], polyurethane (PU) [135], poly(ethylene glycol) methacrylate (PEGMA) and pentaerythritol triacrylate (PETRA) [144], and synthesized ionic liquids (IL) [309], and EG Silicone [243]. In the case of bar microextraction (BaμE) coated with an N-vinylpyrrolidone polymer (NVP) [137] and polystyrene-divinylbenzene (PS-DVB) [300], the recoveries obtained with the method developed here were also better, except for CBZ with BaμE (NVP) [137]. Similar recoveries were obtained by using rotating disk sorptive extraction (RDSE) coated with OASIS HLB [29, 306], a sorbent phase widely used in SPE to preconcentrate PPCPs, and a microextraction bar (BaμE) coated with a synthetic polymer (P5) [136]. In an attempt to explain these results, we compared the amount of the sorbent phases used and their physic and chemical properties in the different studies. The results, which are presented in Table 4.10, show that smaller amounts of sorbent phase, such as those reported in [135, 137, 139, 144, 308, 309], led to lower recoveries being obtained, except in the case of BAμE (P5) and BaμE (NVP). Both polymeric-based (P5 and NVP) allowed an improvement in the sensitivity and selectivity of HPLC-DAD determination given that sorption mechanisms include hydrophobic and π-π interactions. The LODs achieved by the developed method are almost as good as those of other microextraction techniques using the same instrumental system [135] despite, the desorption conditions and the characteristics of the sorbents used

being different. Furthermore, our method has the advantage of its simplicity and the use of a commercially available sorbent. The LODs obtained can be improved by reducing the desorption volume, although this reduction is limited by the need for the SR to be completely immersed in the desorption solvent, or by evaporating the methanol extract until dryness and then reconstituting the solution with a lesser volume of solvent. When more sensitive instrumental techniques, such as liquid chromatography tandem mass spectrometry (LC-ESI-MS/MS) and gas chromatography-mass spectrometry (GC-MS), are used in combination with SBSE coated with PDMS, EG silicone, BAμE (NVP), and BAμE (PS-DVB), the LODs were lower than those obtained with the developed method [29, 144, 243, 290, 306, 308]. The combination of the proposed methodology based on the use of a commercial SR with LC-MS/MS will result in a suitable method having sufficient sensitivity as to be applied in the monitoring of NAP, KET, DCF and TCS in surface waters

4.2.7. Real sample analysis

The developed method was applied to the analysis of river water samples (Table 4.11). TCS was detected in the three river waters at concentration levels of approx. 1.4, 1.3 and 1.7 $\mu g.L^{-1}$, respectively, and DCF was detected at 1.1 and 1.7 μgL^{-1} in two samples, whereas NAP, KET, CBZ were not detected. All these values are higher than the LODs of both analytes but they were close or lower of the LOQs. Figure 4.15 shows the chromatograms of (a) a standard solution and (b) one of the samples. Ginebreda et al. [45] found that the mean concentration levels of DCF in surface water of the Llobregat river in Spain was of 2.20 $\mu g.L^{-1}$ with a maximum DCF concentration of 18.74 $\mu g.L^{-1}$. These values are higher than the DCF concentrations found in Fluvià and Ter river water.

Table 4.10. Comparison of the LODs and average recovery of different static microextraction techniques for the determination of PPCPs.

PPCPs	Static microextraction technique	Instrumental technique	Recovery (%)	LOD ($\mu g.L^{-1}$)	Amount (g) or µL	Ref.
NAP	BAµE (P5)	HPLC-DAD	100.1	0.025	0.001	[136]
	SBSE (IL)	HPLC-UV	52.7	0.31	30 µL	[309]
	SBSE (PDMS) SBSE (PU)	HPLC-DAD	9.8 78.3	1 0.4	0.1201 0.1	[135]
	RDSE (Oasis™ HLB)	GC-MS	94	0.007	0.06	[29]
	RDSE (Oasis™ HLB)	UHPLC–ESI–TOF/MS	98.6	0.003	0.05	[306]
	SBSE (PDMS)	GC-MS	15.5	0.034	0.1201	[308]
	SR (PDMS)	**HPLC-DAD**	**86.53**	**0.56**	**0.037**	**This study**
KET	BAµE (P5)	HPLC-DAD	101	0.05	0.001	[136]
	SBSE (IL)	HPLC-UV	51.6	0.27	30 µL	[309]
	SBSE (PDMS)	GC-MS	21.2	0.01	0.1201	[308]
	RDSE (Oasis™ HLB)	GC-MS	104	0.011	0.06	[29]
	RDSE (Oasis™ HLB)	UHPLC–ESI–TOF/MS	107.8	0.002	0.05	[306]
	SR (PDMS)	**HPLC-DAD**	**96.1**	**1.02**	**0.037**	**This study**
DCF	BAµE (P5)	HPLC-DAD	99.1	0.1	0.001	[136]
	BAµE (NVP)	HPLC-DAD	87.4	0.02	0.0025	[137]
	SBSE (PDMS) SBSE (PU)	HPLC-DAD	34.6 77.7	1.6 0.7	0.1201 0.1	[135]

Table 4.10. Comparison of the LODs and average recovery of different static microextraction techniques for the determination of PPCPs. (continued)

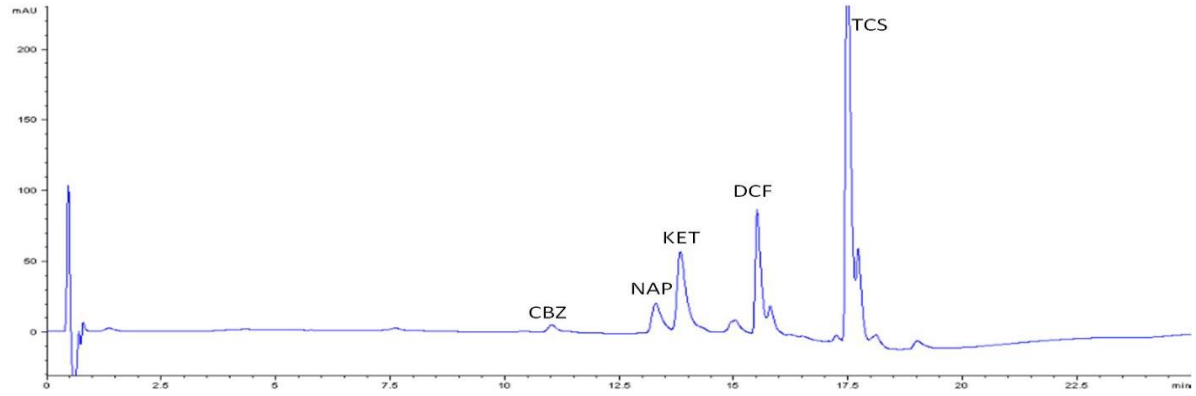
PPCPs	Static microextraction technique	Instrumental technique	Recovery (%)	LOD ($\mu g.L^{-1}$)	Amount (g) or µL	Ref.
	SBSE (PDMS)	GC-MS	21.0	0.037	0.1201	[308]
	Silicone rod	LC-MS/MS	-	16	0.288	[142]
	SBSE (poly(PEGMA-co-PETRA)	LC-MS/MS	33	0.05	225 µL	[144]
	RDSE (Oasis™ HLB)	GC-MS	71	0.033	0.06	[29]
	RDSE (Oasis™ HLB)	UHPLC–UESI–TOF/MS	95.1	0.089	0.05	[306]
	SR (PDMS)	**HPLC-DAD**	**103.98**	**0.75**	**0.037**	**This study**
CBZ	BAµE (NVP)	HPLC-DAD	102.4	0.02	0.0025	[137]
	SBSE (poly(PEGMA-co-PETRA)	LC-MS/MS	25	0.02	225µl	[144]
	BAµE (PS-DVB)	LVGC-MS	83.3	0.005	0.005	[290]
	Silicone rod	LC-MS/MS	-	14	0.288	[142]
	SR (PDMS)	**HPLC-DAD**	**99.07**	**3.40**	**0.037**	**This study**
TCS	SBSE (poly(PEGMA-co-PETRA	LC-MS/MS	55	0.02	225µL	[144]
	SBSE (EG Silicone Twister®)	LC-MS/MS	80	0.01	32µL	[243]
	SBSE (PDMS)	LC-DAD	78.5	0.1	0.1201	[139]
	BAµE (NVP)	HPLC-DAD	74.5	0.03	0.0025	[137]
	BAµE (PS-DVB)	GC-MS	97.3	0.005	0.005	[290]
	SR (PDMS)	**HPLC-DAD**	**109.45**	**0.47**	**0.037**	**This**

study

Table 4.11. Concentrations (n=2) measured in River water Ter, Fluvià and Onyar with the SR.

PPCPs	Concentration (µg.L^{-1})					
	River water Ter	**RSD (%)**	**River water Fluvià**	**RSD (%)**	**River water Onyar**	**RSD (%)**
CBZ	<LOD	_	<LOD	_	<LOD	_
NAP	<LOD	_	<LOD	_	<LOD	_
KET	<LOD	_	<LOD	_	<LOD	_
TCS	~1.4	3.0	~1.3	28.9	1.7±1.5	2.3
DCF	1.1±0.3	0.2	1.7±2.3	1.5	_	_

(a)



(b)

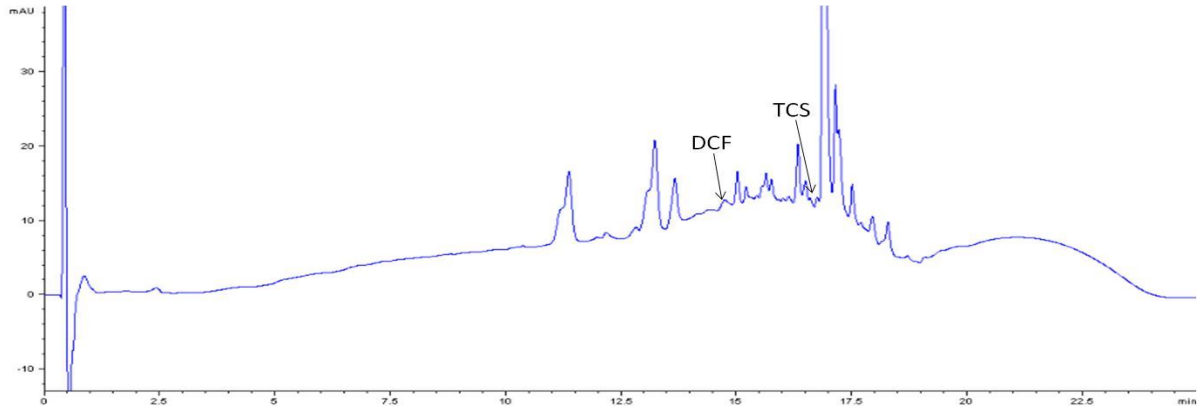


Figure 4.15. (a) Chromatogram obtained of a standard solution containing 100 µg.L^{-1} of the PPCPs extracted with rod. (b) Chromatogram of a river water sample from Fluvià river obtained after extraction with SR.

4.2.8. Summary

A simple, sensitive, effective and low-cost method, based on the combination of PDMS rod extraction with HPLC-DAD has been developed for the determination of four pharmaceutical compounds (NAP, KET, CBZ, DCF) and one ingredient of cosmetic products (TCS) in surface water samples. The different parameters affecting the sensitivity of the method were studied in order to find the best conditions, resulting in detection limits in the 0.47 to 1.02 µg.L^{-1} range, except 3.40 µg.L^{-1} for CBZ. The method has good intraday precision with RSD% in the 0.4– 9.7% range. The highest enrichment factors were obtained for TCS and DCF, which are the most hydrophobic compounds. The LODs of this method can be improved by using a lower volume of the desorption solvent. The use of very small amounts of solvents makes this method also environmentally friendly. The method was validated by analysing spiked river water samples at three concentration levels and obtaining quantitative recoveries and so could then be applied to the analysis of surface water samples. The main advantages of silicone rods are that they are more economical than other sorbents and are single use, so avoiding carryover and contamination issues and allowing HPLC-DAD, which is widely available in non-specialised laboratories, to be used for PPCP determination.

4.3. Granulated cork as biosorbent for the removal of phenol derivatives and emerging contaminants

4.3.1. Precedents

The majority of micropollutants have not been identified as targets of conventional wastewater treatment plants (WWTPs). Process optimization (e.g. increasing sludge residence times), coagulation-flocculation and advanced technologies, such as reverse osmosis and ozonation and other advanced oxidation processes (AOP), are able to remove micropollutants from water, although their high cost limits the degree to which they are employed and, in the case of AOP, toxic intermediate by-products can be generated [148]. A less costly, simple and efficient alternative is the use of adsorption processes, which are able to remove a variety of metallic and organic compounds from aqueous systems. Given its high adsorption capacity, granulated or powdered activated carbon has become the most widely used adsorbent [20]. However, the need to constantly regenerate spent carbon, makes this material costly also in scaled-up use. Activated carbon can be obtained from different waste and natural materials such as pine bark, sawdust and cork bark among others [162]. Granular activated carbon (GAC) obtained from coal, coconut and wood has been used to remove phenols such as 2,4-dichlorophenol [163], and high surface area carbon adsorbents have been synthesized from pine-sawdust and applied to NSAIDS sorption [164].

The direct use of biosorbents, including agriculture wastes, seaweed, fungal biomass, etc., is a low-cost alternative to activated carbon and their uptake capacities can be improved by physical or chemical modification of these biomaterials [177, 178]. Among them, lignocellulosic materials, which are derived from plants, have been widely studied to develop cost-efficient sorbent materials for the removal of metals and phenolic derivatives [180]. Some of these natural materials, such as almond shells, have proved to be particularly efficient in adsorbing PCP (93%) [181] and pomegranate peel and banana peel are also efficient in adsorbing, 2,4-DCP and Ph, respectively [182, 183].

Cork has been used as a biosorbent for pollutants, such as insecticides, uranium, volatile phenols, paracetamol, chloroanisoles, polycyclic aromatic hydrocarbons, and heavy metals. Granulated cork has also proved to be able to remove IBP, CBZ and clofibric acid (CA) from water and wastewater [190]. The interactions of cork with organic pollutants, which are essentially hydrophobic, are explained by the aromatic rings and carboxyl and hydroxyl groups of suberin and lignin. In the case of highly hydrophobic pesticides ($\log K_{ow} > 4$), such as chlorpyrifos, it has been established that raw cork is suitable for their retention. However, adsorption is less successful in the case of hydrophilic pesticides ($\log K_{ow} < 2$), such as methomylandoxamyl [193]. Moreover, the aromatic components of lignin interact with the

aromatic moieties of the adsorbed compoundsvia π-π interactions, as is the case in paracetamol and phenanthrene sorption [194, 195].

The main objectives of this study are (i) to evaluate the sorption capacity of granulated cork towards regulated phenolic compounds (phenol (Ph), 2-chlorophenol (2-CP), 2-nitrophenol (2-NP), 2,4-dichlorophenol (2,4-DCP), pentachlorophenol (PCP), anddiclofenac (DCF)) and emerging contaminants (triclosan (TCS), naproxen (NAP), ketoprofen(KET), carbamazepine (CBZ), and methyl paraben (MPB)); (ii) to study the effect of several parameters, such as pH, compound concentration, and amount of cork on the efficiency of the adsorption process; and (iii) to characterize the sorption processes by analysing the experimental data by the Langmuir and Freundlich isotherm models. The results obtained are compared with the sorption capacities of other biosorbents and biosorbent-based activated carbons.

4.3.2. Characterization of the sorbent (cork structure and morphology)

Cork is mainly composed of two hydrophobic biopolymers, suberin and lignin, and hydrophilic polysaccharides cellulose and hemicellulose. Although highly variable with tree maturity and geographical area, the typical chemical composition of cork is approximately 40% of suberin, 22% lignin, 18% polysaccharides and 15% extractives. The content of suberin is the chemical fingerprint of cork and it is directly related to most of its typical properties [310].

The structural features of cork were observed by SEM at different magnifications. The irregular shape of the granulated cork particles can be observed in the Fig. 4.16A. The structure of cork is compact and presents a regular arrangement of cells without intercellular spaces. The aspect of this arrangement in the transverse section (the plane perpendicular to the plant axis) is similar to a brick-wall and the cells present a rectangular form (Fig. 4.16B) while in the tangential section (the plane perpendicular to a radius) the cork cells appear polygonal, mostly as hexagons with an alveolar (honeycomb-like) structure (Fig. 4.16A).

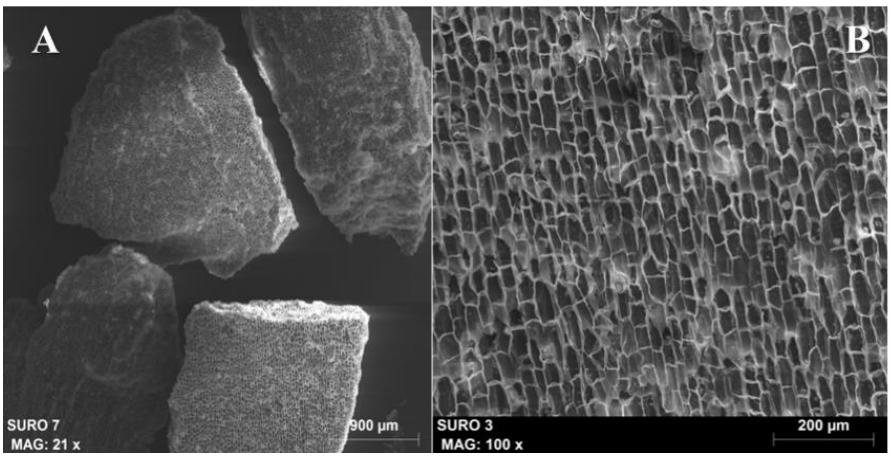


Figure 4.16. Scanning electron micrographs (SEM) of cork granules. A) SEM 21x and B) 100x.

SEM observation of cork also showed that, in a radial section, cork cells predominantly appear as 4, 5 and 6-sided polygons shapes (Fig. 4.17A). On average the cell prism height is 30–40 µm and the cell wall thickness 1–1.5 µm (Fig. 4.17B). An important characteristic of prismatic cork cells is that their lateral faces are corrugated (Fig. 4.17B), with two or three complete corrugations per cell that probably result from compression during cell and bark growth.

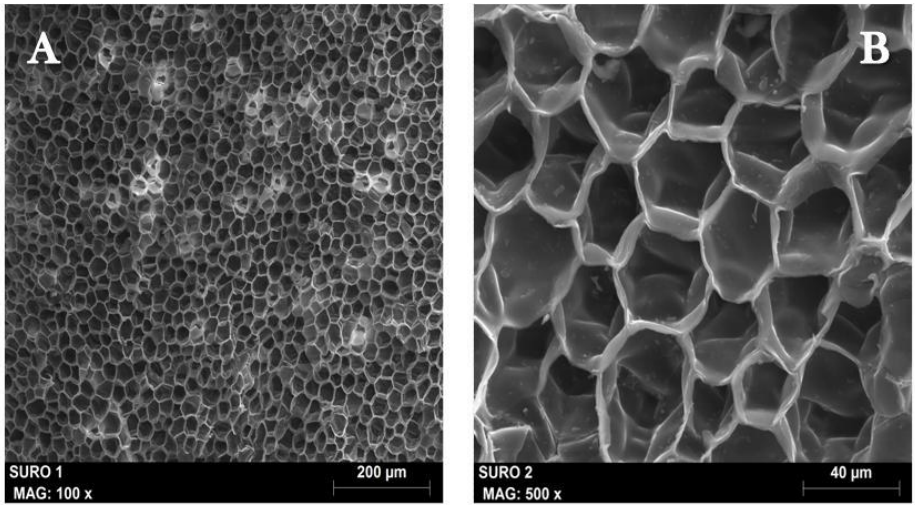


Figure 4.17. Scanning electron micrographs (SEM) of cork granules. A) SEM 100x and B) 500x.

The granulated cork used in this study was sieved to obtain particle sizes smaller than 2mm but due to its irregular shape some larger particles could cross the sieve. Particle size distribution was obtained from the SEM images from measuring the areas of the particles (see

Fig. 4.18 A) an applying a statistical calculation. As can be seen in the Fig. 4.18 B, 94% of the particles have diameters within 2.25–3.5 mm.

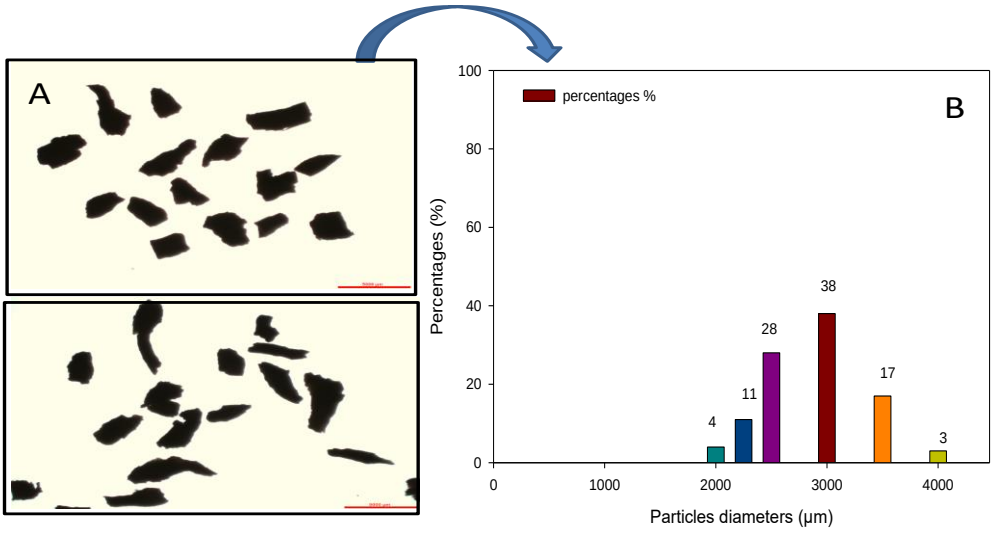


Figure 4.18. Particle size distribution. A) pictures from SEM micrographs, B) Particle size distribution of 8 micrographs.

Surface area for 1-2 mm granulates was 16.3 $m^{2}.g^{-1}$ and for 3-4 mm granulates 10.7 $m^{2}.g^{-1}$. The mean pore diameter was calculated to be around 1-1.34 mm, which indicates the presence of macropores. The pore volume was 2.83 $cm^{3}.g^{-1}$ for 1-2 mm granulates and 2.24 $cm^{3}.g^{-1}$ for 3-4 mm granulates [192]. The fact that surface area and pore volume decrease when the particle size decreases confirms that the cork cells are closed making the interior spaces inaccessibles and only the external surface area is available for sorbing the contaminants.

The apparent porosity is quite large, due not only to inter-granules void space but also to the porous cellular surface. The extensively porous nature of this material is also responsible for a very low bulk density that can vary by as much as a factor of 2 (120–240 $Kg.m^{3}$), depending mostly on its age (virgin or reproduction) and treatment (natural or boiled).

4.3.3. Equilibrium contact time and kinetic studies

The adsorption process was almost complete after 30 minutes for the two groups of micropollutantsand this length of time was chosen for performing the subsequent adsorption experiments (Figure 4.19 and Figure 4.20). The amount of adsorbed compound at the equilibrium, q_e ($mg.g^{-1}$), was calculated by:

$$q_e = \frac{(C_0 - Ceq)\cdot V}{W} \qquad (4.3)$$

where C_0 and C_{eq} ($mg.L^{-1}$) are the liquid-phase concentrations of the target at the initial and equilibrium times, respectively. V (L) is the volume of the solution, and W (g) is the mass of dry adsorbent used.

For both groups of compounds, the decay in the concentration presents an initial stage where the slope is particularly steep, followed by a second period in which the concentration slightly decreases until equilibrium is reached. In the case of the phenolic compounds, equilibrium is reached after 5 minutes (Figure 4.19) and the slope is steeper than in the case of the other group of micropollutants, which attained equilibrium conditions in approximately 30 minutes.

The amount of cork has an important effect on its adsorption capacity towards phenolic compounds. When 100 mg of cork were put in contact with a solution containing 10 $mg.L^{-1}$ of phenolic compounds at pH 6, the percentages of adsorption were 8% for Ph, 15% for 2-CP, 20% for NP, 45% for 2,4-CP, and 75% for PCP as can be seen in table 4.12. These values are lower than those obtained with 200 mg of cork in the same conditions (20% for Ph, 40% for 2-CP, 50% for NP, 75% for 2-4-CP and 100% of PCP). Although the uptakes for each compound are approximately the same (0.2 $mg.g^{-1}$ for Ph, 0.53 $mg.g^{-1}$ for 2-CP, 0.75 $mg.g^{-1}$ for 2-NP and 1.6 $mg.g^{-1}$ for 2,4-DCP).

Figure 4.20 shows that the removal increased as the cork mass was reduced from 10 to 5 mg. The removal percentage for NAP and KET increased from 75% to 82% and from 52% to 57%, respectively, but in the case of CBZ and MPB, removal remained almost the same (Table 4.13). The initial concentration of CBZ and MPB fell by about 70% in the first 5 minutes, but a part of these compounds was desorbed from the cork leaving the remaining concentrations of the two both compounds at around 45% of the initial concentrations. We can assume that TCS and DCF must have been completely adsorbed by the cork since these compounds were not detected in the aqueous solution. Dordio et *al.* have reported higher removal percentages for CBZ (68.1%–87.9%), using different experimental conditions: a broader range of initial concentrations from 1 to 35 $mg.L^{-1}$, granulated cork with larger diameters (from 2.83 mm to 5 mm) and a higher solid-to-liquid ratio of 100 $g.L^{-1}$ [190].

The percentage of adsorption of CBZ, NAP, KET and MPB by cork seems not to depend on the amount of cork used (Table 4.13) although there are some significant differences in the case of CBZ and MPB between the results obtained using 7.5 mg of cork. Rather, and as can be seen in this table, the uptake values decreased to half proportionally when the amount of sorbent was doubled.

The removal percentages obtained in this study for solutions containing $mg.L^{-1}$ are higher than those reported for different types of powdered activated carbon (PAC), which were of 63%, 32% and 31% for CBZ, DCF and KET, respectively [311]. These results were obtained by using $10mg.L^{-1}$ of PAC and in our case the sorbent concentration was of 250 $mg.L^{-1}$. Triclosan is the only studied compound that presented removal percentages as high as 92% by PAC, whereas pharmaceuticals were partially removed [312].

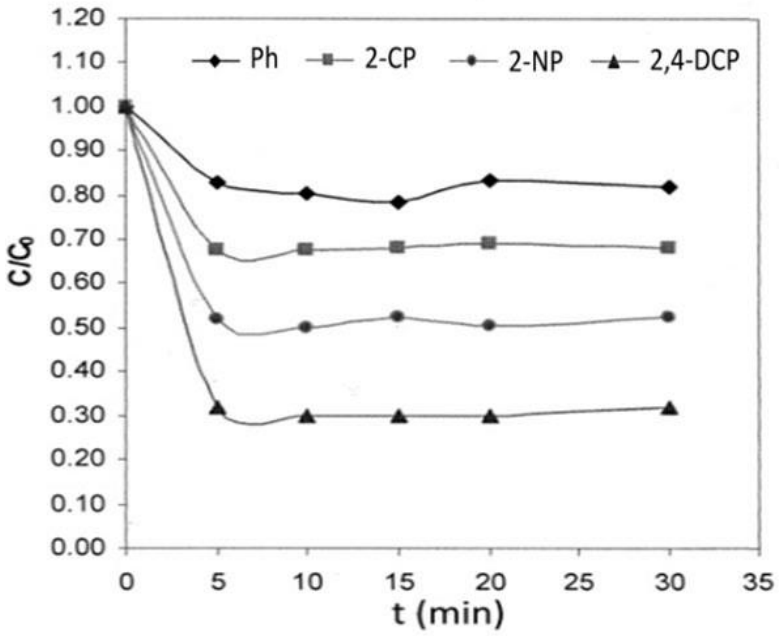
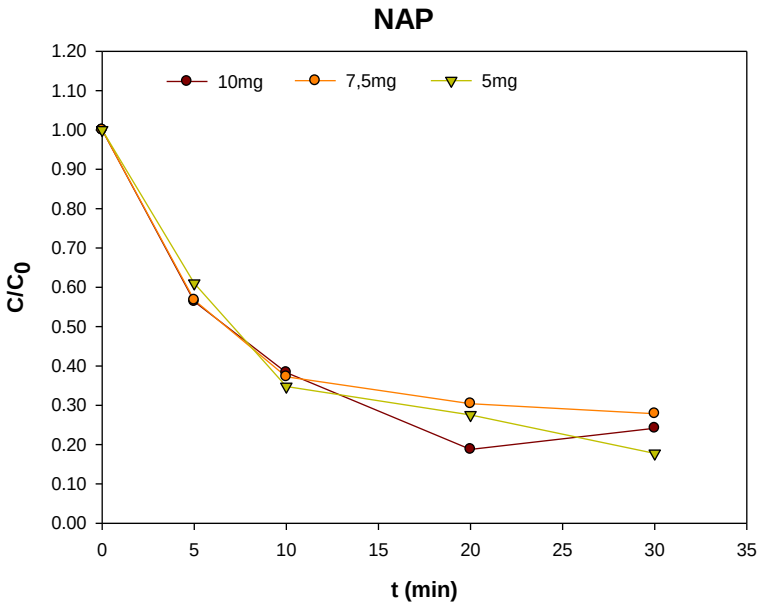
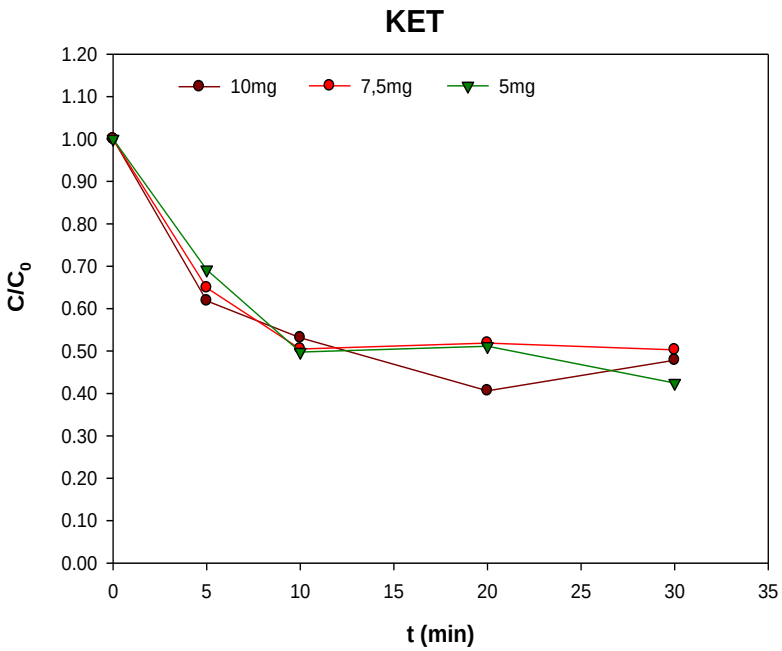


Figure 4.19. Adsorption kinetics. Initial phenolic compound concentration: 30 $mg.L^{-1}$ at pH 6.


NAP
10mg
7,5mg
5mg
C/C0
t (min)
1.20
1.10
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0
5
10
15
20
25
30
35


KET
10mg
7,5mg
5mg
C/C0
t (min)
1.20
1.10
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0
5
10
15
20
25
30
35

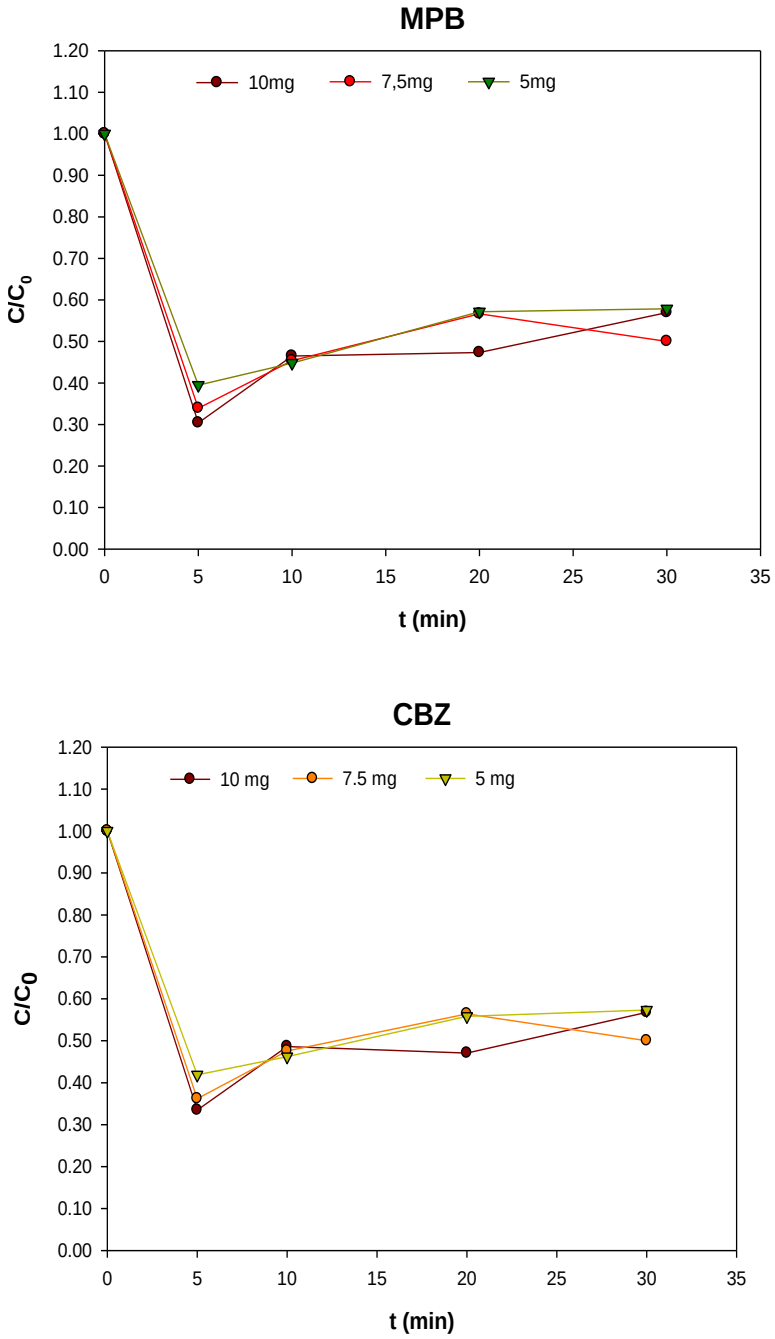


Figure 4.20. Adsorption kinetics of NAP, KET, CBZ and MPB with different amounts of cork. Initial concentration: 1 mg.L^{-1} at pH 6.

4.3.4. Parameters affecting cork sorption: The effect of initial pH and initial concentration

The hydrophobicity of cork explains its high affinity for organic compounds that can be effectively adsorbed when they are present in their non-ionized form in the aqueous solution. Hence, the adsorption of phenolic compounds and the other target micropollutants, except

CBZ, is highly pH dependent, sinceat pH > pKa (Table 1.1), the concentration of negatively charged carboxylate and phenoxide ions increases, whereas at pH < pKa all the target compounds were present in their neutral form. The effect of pH on the removal percentages of cork was studied at pH 4, 6 and 11 (Table 4.12). As can be seen in this table, a significant decrease in the percentage of adsorption of phenolic compounds by cork and in the uptake values were observed at pH 11 due to the increase in the concentration of the ionized organic forms, which have higher solubility than the neutral compound in water. Between pH 4 and 6, no significant differences in terms of removal percentages were observed as all the compounds are protonated. Hence, isotherm experiments were conducted at pH 6 for both groups of compounds although KET, NAP and DCF were present in their ionized forms, this did not affect the adsorption efficiency since uptake was mainly via π-π interactions. The adsorption of TCS by AC is pH dependent and efficiencies of around 60% between pH 3 and 6, that decreased until 15% at pH 11 have been reported [312].

Table 4.12. Effect of the pH on the adsorption of phenolic compounds by cork. Initial concentration: 30 $mg.L^{-1}$, amount of cork: 200 mg.

	Ph		**2-CP**		**2-NP**		**2,4-DCP**	
pH	**%Removal (n=2)**	**q($mg.g^{-1}$) (n=3)**	**%Removal (n=2)**	**q($mg.g^{-1}$) (n=3)**	**%Removal (n=2)**	**q(mg/g) (n=3)**	**%Removal (n=2)**	**q(mg/g) (n=3)**
6	20±0.5	0.63±0.02	45±0.3	1.47±0.03	55±0.3	1.25±0.09	75±0.4	1.61±0.14
4	20±0.3	-	40±0.2	-	55±0.4	-	80±0.2	-
11	10±0.2	0.07±0.02	8±0.2	0.06±0.03	10±0.3	0.1±0.02	8±0.2	0.09±0.03

4.3.5. The influence of the chemical characteristics of the adsorbate

The interactions of cork with organic pollutants, which are essentially hydrophobic, are explained by the aromatic rings and carboxyl and hydroxyl groups of suberin and lignin. In the case of highly hydrophobic pesticides ($\log K_{ow} > 4$), such as chlorpyrifos, it has been established that raw cork is suitable for their retention. However, adsorption is less successful in the case of hydrophilic pesticides ($\log K_{ow} < 2$), such as methomylandoxamyl [193]. Moreover, the aromatic components of lignin interact with the aromatic moieties of the adsorbed compounds via π-π interactions, as is the case in paracetamol and phenanthrene sorption [194, 195]. These findings have been confirmed by molecular modelling calculations, which reveal that π stacking, reinforced by hydrogen bonding, is the main contributor to the interaction between pesticides and lignin [193].

Figure 4.21 and Figure 4.22 show that the amount adsorbed at equilibrium (q_e) increases at greater equilibrium concentrations (C_{eq}). Moreover, as shown in Figure 4.22 the amount adsorbed at equilibrium increases steadily as the amount of cork is decreased. Adsorption isotherms are classified following Giles [313], who identifies four different isotherm shapes (L, H, C and S) by their initial slopes that are dependent on the rate of change of site availability as the amount of solute adsorbed increases.

S-type curves have a concave shape at low concentrations, which indicates an initial competition of solvent and solute molecules for the active points of the sorbent surface, whereas both H and L present a convex shape, which can be explained by the fact that the adsorbed molecules lie flat on the adsorbent surface and, in the case of H isotherms, the affinity increases as the solute concentration decreases. C isotherms are defined by a constant sorption affinity, expressed as a straight line in s vs. c plots. Subgroups of each type are defined by the sorption behaviour at high concentrations while subgroup 2 is characterized by oneplateau; subgroup 1 shows no plateau at all [314].

The slightly concave shape that can be observed in Figure 4.21 for all phenolic compounds except Ph at low concentrations seems to indicate S-shaped curves. This implies a side-by-side association between adsorbed molecules, helping to hold them to the surface, which has also been reported for monofunctional phenols [313]. PCP, 2,4-DCP, 2-CP, 2-NP and Ph present an inflexion point, which implies a change in the slope that is clearer in the case of

PCP than Ph. All the isotherm curves obtained for the phenolic compounds reached a plateau (S2), representing first degree saturation or complete monolayer coverage.

On the other hand, C-shaped curves show a linear relationship between the quantity adsorbed and the amount of sorbent without the system becoming saturated. The linearity demonstrated that the number of adsorption sites of the substrate remains constant. CBZ, MPB, KET, NAP and DCF present C-shape curves (Figure 4.22).

It can be deduced from Figure 4.21 that the adsorption of phenolic compounds follows the sequence PCP > 2,4-DCP > 2-NP > 2-CP > Ph and that this sequence is the same at the different pHs (4, 6 and 11) and amounts of cork (100 and 200 mg). This result is due to the fact that the phenolic derivatives with electronegative substituting groups in the aromatic ring act as Lewis acids [315] and that the aromatic structure of lignin can be viewed as Lewis bases [193]. Therefore, the greater the electronegativity of the substituting groups in the aromatic ring, the greater the extent to which the given compound is adsorbed. A higher degree of halogenation results in a higher level of adsorption (Figure 4.21), which is related to its greater hydrophobicity, whereas since the nitro group is more electronegative than the chlorogroup [316], 2-NP is more adsorbed than 2-CP.

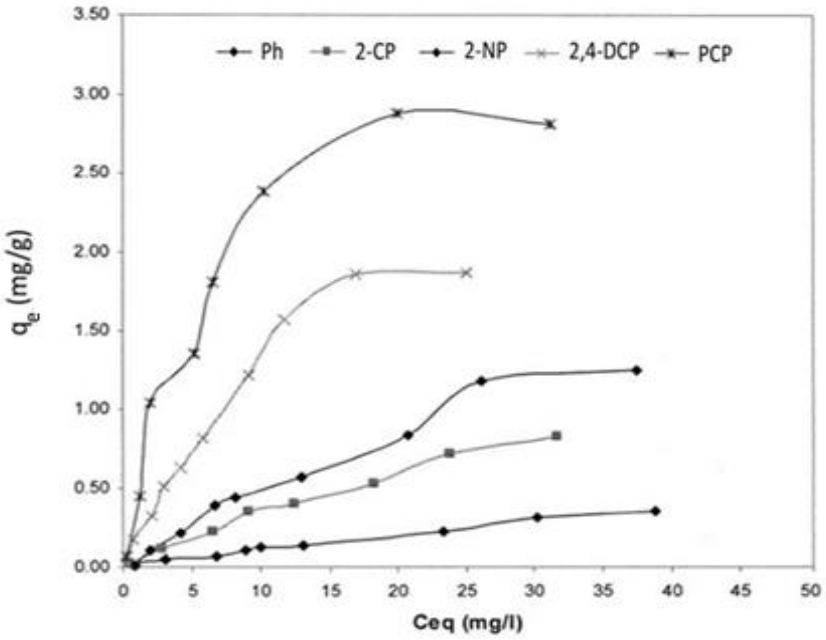


Figure 4.21. Adsorption isotherms of phenols at pH=6 at initial concentrations ranging from 5 to 50 mg.L^{-1} and 200 mg of cork.

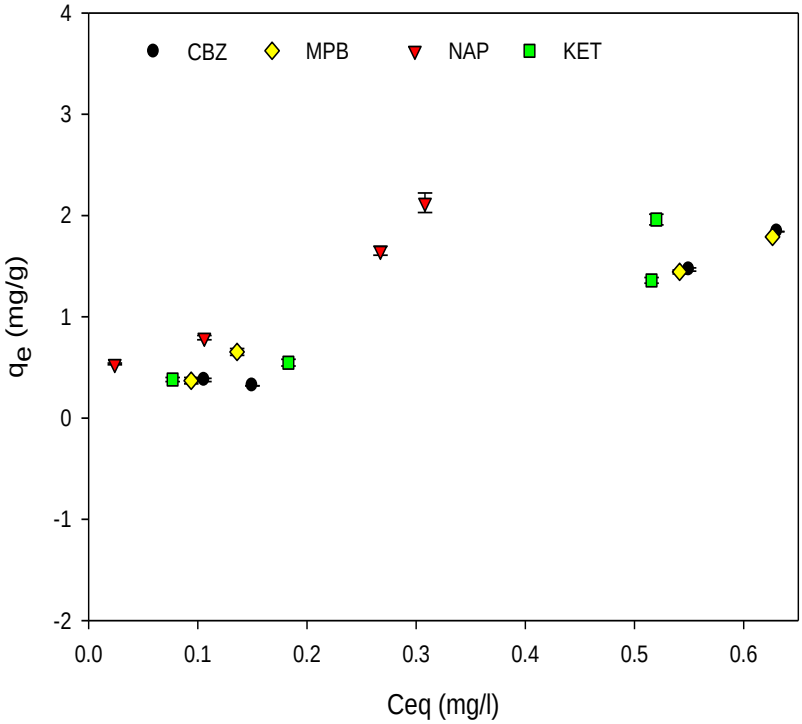


Figure 4.22. Adsorption isotherms of CBZ, NAP, KET and MPB. 1 mg.L^{-1} and 0.5 mg.L^{-1} at pH=6 at different amounts of cork (5, 7.5 and 10 mg).

In the case of the emerging contaminants tested, the adsorption capacities followed their order of hydrophobicity: TCS and DCF > NAP > KET > CBZ and MPB. In the case of NAP and KET, which have similar $\log K_{OW}$, the higher adsorption capacity obtained by NAP in comparison with KET (see Table 1.1) can be explained by the higher water solubility of the latter. Moreover, the hydrophobic interaction of these compounds with the cork are complemented by the π–π interactions between the aromatic moieties of the compounds and the aromatic rings of lignin [193]. The π–π interaction has been found to be a driving force of enhanced sorption of aromatic compounds, such as phenolic derivatives by soil organic matter [316] and the adsorption of pharmaceutical compounds, such as DCF by activated carbon [317].

Table 4.13. Effect of amount of cork on pharmaceutical and cosmetic products removal at pH=6. Initial concentration: 1mgL^{-1}.

	%Removal (n=2)	**uptake q(mg.g^{-1})**	**%Removal (n=2)**	**uptake q(mg.g^{-1})**	**%Removal (n=2)**	**uptake q(mg.g^{-1})**
Amount of cork	**5mg**	**5mg**	**7.5mg**	**7.5mg**	**10mg**	**10mg**
CBZ	42±0.08	1.84	50±1,46	1.46	43±0.88	0.93
NAP	82±1.86	3.56	72±8.76	2.12	75±3.93	1.65
KET	57±3.15	2.31	50±5.11	1.35	52±2.7	1.05
MPB	42±0.01	1.78	50±1.86	1.44	43±1.48	0.91
TCS	100*	-	100*	-	100*	-
DCF	100*	-	100*	-	100*	-

*Non-detectable concentrations in the aqueous solution.

4.3.6. Adsorption isotherms

Langmuir and Freundlich models are typically used to indicate the interaction between the sorbent and the adsorbate when the adsorption process reaches equilibrium. The Langmuir isotherm theory assumes monolayer coverage of adsorbates over homogeneous adsorbent surfaces, which can be characterized as a plateau. Therefore, at equilibrium, a saturation point is reached where no further adsorption can occur. Moreover, the Langmuir model [318] considers that the ability of a molecule to be adsorbed at a given site is independent of the occupation of neighbouring sites and the isotherm equation representing the adsorption of one solute from a liquid [319, 320] is expressed by the following equation:

$$q_e = \frac{Q_{max}\ K_L\ Ce}{1+K_L\ Ce} \qquad (4.4)$$

Where q_e is the amount (mg.g^{-1}) of adsorbed compound at equilibrium, C_{eq} is the equilibrium concentration (mg.L^{-1}) and K_L (L.g^{-1}) and Q_{max} (maximum adsorption capability, mg.g^{-1}) are the Langmuir constants of adsorption. K_L and Q_{max} can be determined by fitting the experimental data to the linearized equation derived from eq (2):

$$\frac{1}{q_e} = \frac{1}{Q_{max}} + \frac{1}{C_{eq} \cdot Q_{max} \cdot K_L} \qquad (4.5)$$

The empirical Freundlich model is based on multilayer adsorption on heterogeneous surfaces. The equation is commonly described as follows [319, 320]:

$$q_e = K_F \cdot C_{eq}^{1/n} \qquad (4.6)$$

and its logarithmic form is expressed as:

$$\log q_e = \log K_F + \frac{1}{n} \log C_{eq} \qquad (4.7)$$

where K_F ($L^{1/n}$ $mg^{(1-1/n)}$ g^{-1}) represents the sorption capacity when the equilibrium concentration equals 1mg.L^{-1} and it is characteristic of the sorption system (adsorbent and adsorbate).1/n is a function of the strength of adsorption in the adsorption process and will normally range from 0.7 to 1.0 [319, 320]. These values show that when the adsorbate concentration increases, the relative adsorption decreases, presumably indicating saturation of the adsorption sites available to the adsorbate. In general, when n values are in the 2–10 range the adsorption is considered to be good whereas when n is in the 1-2 range, sorption is moderately difficult.

The adsorption parameters of the Langmuir and Freundlich models obtained for the adsorption of PPCPs and phenolic compounds on cork are given in Table 4.14, except for TCS and DCF, which were completely adsorbed at the experimental conditions tested. The determination coefficient (r^2) of the Freundlich equation (eq. 5) ranges from 0.94 to 0.99 for all the studied compounds, whereas for phenolic compounds the Langmuir equation (eq. 3) gave ranges from 0.94 to 0.98. Based on the determination coefficients (r^2), the adsorption isotherms for phenolic compounds fit well with both models as is the case when moderate concentration ranges are studied. In the case of the studied emerging contaminants, the experimental data only fits the Freundlich model with r^2 ranging from 0.95-0.98.

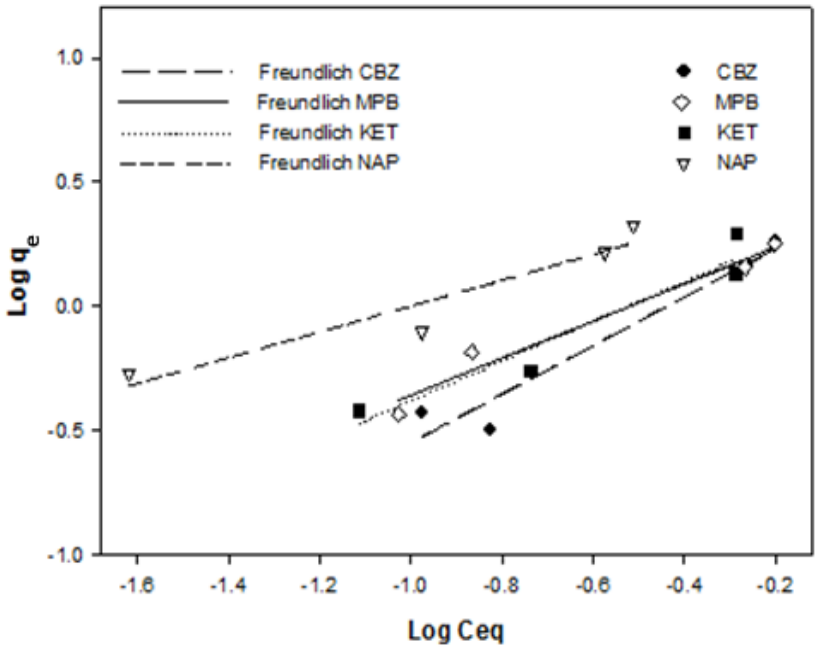


Figure 4.23. Freundlich adsorption isotherms of PPCPs at different amounts of cork.

Table 4.14. Freundlich and Langmuir parameters and correlation coefficients.

Compounds	Freundlich model			Langmuir model		
	K_f	1/n	r^2	Q_{max}	K_l	r^2
Ph	0.02	0.86	0.98	0.92	0.02	0.98
2-CP	0.05	0.81	0.99	1.54	0.03	0.99
2-NP	0.06	0.88	0.98	5.09	0.01	0.99
2,4-DCP	0.20	0.80	0.99	6.24	0.03	0.94
PCP	0.64	0.52	0.92	5.31	0.07	0.95
NAP	3.32	0.52	0.95			
KTP	2.63	0.80	0.96			
CBZ	2.68	0.97	0.97			
MPB	2.45	0.74	0.98			

The Freundlich K_F and Langmuir Q_{max} parameters indicate the affinity of phenolic compounds to cork: the greater the K_F or Q value, the higher the affinity [321]. Hence, PCP and 2,4-DCP have a greater affinity to be adsorbed by cork than Ph, 2-CP and 2-NP (Table 4.14) as has been demonstrated by the values of the uptakes and removal percentages (Table

4.12). Q_{max} represents the theoretical monolayer capacity in the Langmuir model, with the highest value being found for 2,4-DCP. The adsorption isotherms displayed the following order of adsorption capacity: Ph < 2-CP < 2-NP < 2,4-CP < PCP, showing that hydrophobicity and acidity are the main characteristics of phenols and that they play an important role in the adsorption process as was reported in the adsorption of phenols by GAC [320].

The Freundlich 1/n value, which is calculated from the slope of eq. 5, determines the degree of non-linearity between solution concentration and adsorption. Ph, 2-CP, 2-NP, 2,4-DCP, KET, CBZ and MPB present 1/n values close to 1 and n values in the 1.03 to 1.35 range. This steep slope indicates that the higher the equilibrium concentration, the greater the adsorption capacities, although saturation is never reached. With regards to PCP and NAP the 1/n value is lower than 1 (0.5), showing that the adsorptive capacity is only slightly reduced at lower equilibrium concentrations resulting in good sorption systems with n~2.

Adsorption isotherms provide information that is useful for the scaling process and enables the calculation of the theoretical cork dosage that is necessary to remove organic pollutants effectively from contaminated effluent. Table 4.15 shows the amount of cork required to reduce the charge of the compounds that have a higher affinity for cork (2,4-DCP, PCP, NAP, KET, CBZ and MPB) from 1 $mg.L^{-1}$ to 0.1 $mg.L^{-1}$. As can be seen, the lower the Q_{max} and K_F values, the greater the amount of cork required. The results show that cork can be a useful adsorbent for the removal of the most hydrophobic compounds, such as PCP and 2,4-DCP, TCS and DCF, while it is less efficient for the removal of Ph, 2-CP and2-NP. This finding was also reported for the sorption of pesticides by granulated cork, which is governed by the octanol–water partition coefficient of the adsorbed molecules [193].

The estimated adsorption capacities (K_F) and n values for NAP, KET, CBZ and MPB were found to be 3.68, 2.92, 2.96 and 2.72 and 1.98, 1.03, 1.25 and 1.34, respectively (Table 4.15). These results suggest that small amounts of cork possess a relatively high removal capacity for all these compounds, and especially for TCS and DCF, which were completely adsorbed, and for NAP, which gave the highest K_F and n values, following their hydrophobicity order. Moreover, the adsorption process of these compounds is based on the same chemical interactions, such as π-π interactions as adsorption capacities are high despite some of the pharmaceuticals being present in solution in their ionized forms. The sorption of CBZ by

granulated cork and rice straw was reported to follow the Freundlich equation with n= 1.38 [190] and n= 0.926 [188].

Table 4.15. Theoretical amount of cork required to reduce the charge of each phenolic compound from 1 mg.l^{-1} to 0.1 mg.l^{-1} and PPCPs from 1 mg.l^{-1} to 0.1 mg.l^{-1}.

Compounds	Freundlich isotherm	Cork dosage (g.L^{-1})	Langmuir Isotherm	Cork dosage (g.L^{-1})
Ph	q_e=0. 016 $C_{eq}^{1/1.16}$	409	$q_e = \frac{0.92 \times 0.016 \times C_{eq}}{1 + 0.016 \times C_{eq}}$	612
2-CP	q_e = 0.053 $C_{eq}^{1/1.24}$	109	$q_e = \frac{1.54 \times 0.029 \times C_{eq}}{1 + 0.029 \times C_{eq}}$	366
2-NP	q_e = 0.053 $C_{eq}^{1/1.13}$	108	$q_e = \frac{5.09 \times 0.011 \times C_{eq}}{1 + 0.011 \times C_{eq}}$	161
2,4-DCP	q_e = 0.201 $C_{eq}^{1/1.24}$	29	$q_e = \frac{6.24 \times 0.027 \times C_{eq}}{1 + 0.027 \times C_{eq}}$	54
PCP	q_e = 0.637 $C_{eq}^{1/1.91}$	4.72	$q_e = \frac{5.31 \times 0.070 \times C_{eq}}{1 + 0.070 \times C_{eq}}$	24
NAP	q_e = 3.32 $C_{eq}^{1/1.92}$	0.91		
KTP	q_e = 2.63 $C_{eq}^{1/1.25}$	2.16		
CBZ	q_e = 2.68 $C_{eq}^{1/1.03}$	3.13		
MPB	q_e = 2.45 $C_{eq}^{1/1.35}$	2.02		

4.3.7. Comparison of the adsorption capacity of different adsorbents

The adsorption capacity of cork towards phenolic compounds and PPCPs has been compared with those reported for other adsorbents (Tables 4.16 and 4.17). Among them, we selected activated carbon produced from vegetable wastes and various agricultural wastes, as these have a similar origin to cork.

As the adsorption capacity depends on the pH of the solution, the amount and characteristics of the sorbent, the initial concentration of the target, and the contact time, it is very difficult to compare the sorption capacities of different adsorbents. However, we selected the Langmuir parameter, Qmax, to compare the adsorption capacity towards phenolic compounds (Table 4.16) and PPCPs (Table 4.17) by different sorbents.

The Q_{max} values reported for the sorption of phenolic compounds by raw biosorbents such as tendu leaves, seagrass *Posidonia* fibres, and *Cystoseira indica* algae are of the same order as those obtained with granulated cork and granular-activated carbon, except for a seaweed (*sargassummuticum*) [179], *Macrocystis integrifolia Bory* algae [322] and pomegranate and banana peels (Table 4.16) [182, 183]. However, they are, in general, lower than the values obtained with treated biosorbents, such as heat-treated rice husk [177], sugarcane bagasse fly ash [179], and carbons obtained from oil palm empty fruit bunches [177], palm pith [183], maize cob [323], and corn wastes [90]. Granulated cork has a higher affinity to 2-CP than heat-treated rice husk [177] and similar affinity to this compound as granulated activated carbon [179]. The affinity of granulated cork to 2,4-DCP is lower than those presented by activated carbons prepared from vegetable wastes [178, 183, 323] and higher than seagrass *Posidonia oceanica (L.*) fibres [90]. However,similar affinities to PCP are found for granulated cork and AC from corn cobs [324]. In the case of 2-NP, cork is less efficient than *Macrocystis integrifolia Bory* algae and technically hydrolysed ligninin adsorbing this compound [322, 325]. In general, activated-carbons produced from vegetal wastes resulted in higher Q_{max} values, in the 100-300 $mg.g^{-1}$ range, for phenolic compound sorption [178].

It was not possible to calculate Qmax in the case of NAP, KET, CBZ and MPB as the adsorption isotherms (Freundlich equation) did not plateau out and, in the case of DCF and TCS, because these compounds are completely adsorbed at the experimental conditions used in this study. The Qmax values obtained in other studies are collected in Table 4.17.

Table 4.16. Comparison of the adsorption capacity of different adsorbents for phenolic compounds.

Adsorbates	Adsorbents	Langmuir Q_{max} ($mg.g^{-1}$)	References
Ph	Granulated cork	0.92	This study
Ph	Rice husk (heat treated)	14.4	[177]
Ph	Sugarcane bagasse fly ash	23.83	[177]
Ph	Tendu leaf (raw)	7.6	[177]
Ph	Rice bran ash (RBA)	4.63	[179]
Ph	Granular activated carbon	4.85	[179]
Ph	*Sargassummuticum* seaweed	2.8	[179]
Ph	*Cystoseira indica* biomass	2.14	[179]
Ph	Banana peel (raw)	688.9	[183]
2-CP	Granulated cork	1.54	This study
2-CP	Rice bran ask	3.66	[179]
2-CP	Rice husk (heat treated)	0.21	[177]
2-CP	Granular activated carbon	4.28	[179]
2-CP	*Cystoseira indica* biomass	2.77	[179]
2-CP	*Sargassummuticum* seaweed	22.0	[179]
2-CP	*Macrocystis integrifolia Bory* algae	24.18	[322]
2-NP	Granulated cork	5.09	This study
2-NP	*Macrocystis integrifolia Bory* algae	97.37	[322]
2-NP	Technical hydrolysed lignin	1.87	[325]
2,4-DCP	Granulated cork	6.24	This study
2,4-DCP	*Posidonia oceanica (L.) seagrass fibers*	1.11	[90]
2,4-DCP	Pomegranate peel	65.7	[182]
2,4-DCP	Palm pithcarbon	19.16	[183]
2,4-DCP	AC fromoil palm empty fruit bunch	27.25	[178]
2.4-DCP	Maize cob carbon	17.94	[323]
PCP	Granulatedcork	5.31	This study
PCP	AC from corn cobs	5.26	[324]

Table 4.17. Comparison of adsorption capacity of different adsorbents for PPCPs.

Adsorbates	Adsorbents	Q_{max}(mg g^{-1})	Ref.
NAP	AC from pine sawdust-*Onopordum acanthium L.*	205.8	[164]
NAP	AC from waste apricot	106.4	[184]
NAP	AC from olive waste	39.5	[184]
NAP	AC from pine chip	290	[184]
NAP	AC from coconut shell	69.96	[187]
KET	AC from olive waste	24.7	[184]
CBZ	Granulated cork	0.37	[190]
CBZ	AC from coconut shell	57.56	[187]
CBZ	Rice straw	40	[188]
DCF	AC from pine sawdust *Onopordum acanthium L.*	263.7	[164]
DCF	Isabel grape bagasse	76.98	[189]
DCF	AC from pine chip	372	[184]
DCF	AC from olive waste	56.2	[184]
DCF	AC from cyclamen tubers	22.22	[184]
DCF	AC from peach stones	200	[184]
DCF	AC from cocoa shell	63.47	[186]
DCF	AC from potato peel waste	68.5	[185]
TCS	charcoal-based AC wastewater	70.42	[326]
TCS	biosolid-derived biochar	0.872	[327]

GAC: granular activated carbon

AC: activated carbon

Few studies have reported the sorption of PPCPs using non-treated vegetable wastes and, in general, activated carbons generated from vegetable wastes are used. The sorption of NSAIDs by this type of activated carbons has been recently revised [184]. AC from pine sawdust and pine chip gave the highest Q_{max} values for NAP and DCF adsorptions and, in the case of AC from pine sawdust, the reported K_F values (46.7 and 56.5) [164] are ten times higher than

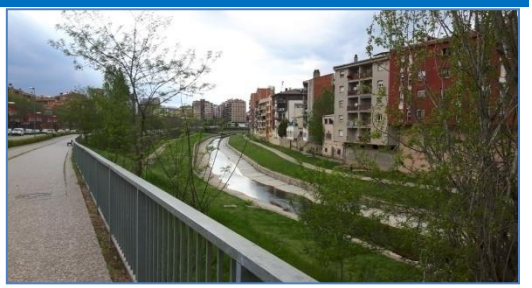
those obtained here with granulated cork as sorbent. The adsorption capacity of KET by olive waste cakes-AC is lower than the Q_{max} values calculated on the adsorption of DCF and NAP for the same sorbent, following the adsorption capacity order reported in the literature [184] for NSAIDs: DCF > NAP > KET. The results obtained in this study, in terms of sorption percentage (Table 4.13) and K_F values, are in agreement with this order. Activated carbons from peach stones, cyclamen tubers and potato peel waste were highly effectives in adsorbing DCF [184, 185] as well as AC from cocoa shell [186] and AC from coconut shell applied to adsorb NAP and CBZ [187]. Wastewater biosolid derived biochar is less efficient than charcoal-based AC in absorbing TCS [326, 327]. Sorption on activated carbon based sorbents is a very effective process in removing some PPCPs from wastewaters, however, their production and regeneration requires energy and, in most cases, the use of chemical products [184, 188]. The direct use of biosorbents can be a cost effectiveness alternatively as it is the case of the removal of DCF by Isabel grape bagasse [189] and CBZ by rice straw [188] and granulated cork [190].

4.3.8. Summary

In this study we have demonstrated that cork can be used as a novel adsorbent of micropollutants, such as phenolic compounds and emerging contaminants. In the case of phenolic compounds, the adsorption is highly dependent on their chemical characteristics and the pH of the solution. Maximum uptake is obtained at pH 6 and it is found that the higher the electronegativity of the substituting groups in the aromatic ring, the greater the sorption capacity of the cork. Conventional Langmuir and Freundlich isotherms satisfactorily fitted the adsorption isotherm data of the five phenolic compounds in cork. Granulated cork also resulted to be an efficient sorbent for DCF, TCS, NAP, KET, CBZ and MPB. In the case of DCF and TCS, 100% removal efficiency was obtained by using 5 mg of cork. PPCP sorption is not dependent on the amount of cork nor on the fact that some of these compounds are present in the solution in their ionized form as the adsorption process is based on the same chemical interactions, mainly π-π interactions.

The great advantage of using powdered or granulated cork as an adsorbent is that in cork-producing areas it is a readily available material that can be acquired at minimal or no cost and which, furthermore, requires no pre-treatment before use. The fact that larger quantities may be required to obtain the same results becomes irrelevant in these circumstances.

5. CONCLUSIONS



In addition to including the conclusions obtained in the different studies of this thesis in each chapter, the main conclusions are summarized below:

- The principles and innovations of sorbent-based microextraction techniques such as solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE), stir-rod-sorptive extraction (SRSE), bar adsorptive microextraction (BAμE), fabric phase sorptive extraction (FPSE) and silicone rod (SR)/silicone tube (ST) extraction have been revised with special emphasis on the determination of pharmaceuticals and ingredients of personal care products. All these techniques have positive features that include simplicity, reduction of extraction time and multistage operations, and a reduction in solvent consumption allowing the use of well-known instrument configurations, such as HPLC-UV/Vis. However, the main drawback of microextraction techniques is selectivity as most of the available sorbents are limited in their capacity to extract highly polar compounds. There is also a clear need for less costly and simpler microextraction techniques based onthe use of bulk materials e.g. silicone rods or silicone tubes. PDMS rod-based materials present similar efficiencies to those obtained by SBSE and meet analytical requirements in terms of purity, inertness and thermal stability. Other advantages of SRs are their greater flexibility and robustness, together with the fact that they can be discarded after a single use, eliminating problems of carry over. Moreover, PDMS tubes can also be used both as partition and permeation sampling devices.

- A simple, sensitive, effective and low-cost method, based on the combination of PDMS rod extraction with HPLC-DAD has been developed for the determination of four pharmaceutical compounds (NAP, KET, CBZ, DCF) and one ingredient of cosmetic products (TCS) in surface water samples.

- The different parameters affecting the sensitivity of the method were studied in order to find the best conditions resulting in detection limits ranging from 0.47 to 1.02 μg.L^{-1} for NAP, KET, DCF and TCS, except for CBZ which was 3.40 μg.L^{-1} as well as greater precision. LOQs ranged from 1.44 to 3.17 μg.L^{-1}, except for CBZ, which was 10.33 μgL^{-1}. The method has good intraday precision with RSD% in the 0.4 to 9.7% range. Enrichment factors of 10 for NAP, 24 for KET, 108 for DCF and

179 for TCS were obtained. The highest enrichment factors were obtained for TCS and DCF as they are the most hydrophobic of the target PPCPs.

- The LODs of this method can be improved by using a lower volume of the desorption solvent although this reduction is limited by the need for the SR to be completely immersed in the desorption solvent or by evaporating the methanol extract until dryness and then reconstituting the solution with a lesser volume of solvent. The use of very small amounts of solvent makes this method environmentally friendly.

- The method was validated by analysing spiked river water samples at three concentration levels and obtaining quantitative recoveries of between 84.8 and 111.2% and so this method could then be successfully applied by us to analyse surface water samples.

- When comparing the results obtained in terms of LODs and recovery factors with those of other microextraction techniques sharing similar principles, the proposed methodology was found to have better recovery levels and sensitivities that are close to those of other microextraction techniques using the same instrumental system. Despite the benefits of these other techniques, SR based microextraction has the two important advantages; firstly, that silicone rods are more economical than other sorbents and, secondly, the fact that they are of single use avoids carryover and contamination issues and allows PPCP determination to be performed by HPLC-DAD, which is widely available in non-specialised laboratories.

- Cork, a lignocellulosic hydrophobic material, which contains approximately 45% suberin and 27% lignin, was selected to be evaluated as a biosorbent for phenolic compounds and PPCPs. Granulated cork was characterized by SEM in order to study its structure and particle size distribution. SEM showed that the alveolar (honeycomb-like) structure of the cork material is made up of thin-walled cells that are closed and hollow, forming shapes of predominantly 4, 5 and 6 sided polygons, without intercellular space. The particle size distribution measurements, which were obtained by measuring the particle areas in the SEM images, found 94% of the particles to have diameters between 2.25 and 3.5 mm.

- The capacity of granulated cork to sorb phenolic compounds is highly dependent on the amount of sorbent used, the chemical characteristics of the adsorbates as well as of the pH of the solution. In the case of phenolic compounds, maximum removal percentages of 100% for pentachlorophenol, 75% for 2,4-dichlorophenol, 55% for 2-nitrophenol, 45% for 2-chlorophenol, 20% for phenol were obtained at pH 6 with 200 mg of cork and the initial concentration was of 30 $mg.L^{-1}$. The adsorption of phenolic compounds follows the sequence PCP > 2,4-DCP > 2-NP > 2-CP > Ph. Maximum uptakes of 1.61 $mg.g^{-1}$ for 2,4-dichlorophenol, 1.47 $mg.g^{-1}$ for 2-chlorophenol, 1.25 $mg.g^{-1}$ for 2-nitrophenol and 0.63 $mg.g^{-1}$ for phenol were obtained at pH 6 and it was found that the higher the electronegativity of the substituting groups in the aromatic ring, the greater the sorption capacity of the cork.

- In the case of emerging contaminants, the adsorption capacities followed their order of hydrophobicity: TCS and DCF > NAP > KET > CBZ and MPB with removal percentages of 100% for sodium diclofenac and triclosan, 82% for naproxen, 57% for ketoprofen, and 50% for carbamazepine, and methyl paraben when 5-10 mg of cork was used and the initial concentration was of 1 $mg.L^{-1}$. The high removal efficiencies obtained are explained bythe hydrophobic interactions of cork with organic pollutants, which are complemented by the π–π interactions between the aromatic moieties of the compounds and the aromatic rings of lignin. Maximum uptakes of 3.56 $mg.g^{-1}$ for naproxen, 2.31 $mg.g^{-1}$ for ketoprofen, 1.84 $mg.g^{-1}$ for carbamazepine, and 1.78 $mg.g^{-1}$ for methyl paraben were obtained at pH 6. Uptake values decreased by around 50% when the amount of sorbent was doubled.

- The adsorption isotherm equilibrium data of phenolic compounds and PPCPs were analysed by applying the Langmuir and Freundlich models. Both models fit well with the adsorption experimental data for phenolic compounds whereas in the case of PPCPs, only the Freundlich model fits the experimental data. The adsorption parameters of the Langmuir and Freundlich models: K_F, Q_{max}, 1/n and b values were also calculated.

- Adsorption isotherms also provide information that is useful for the scaling process and enables the calculation of the theoretical cork dosage that is necessary to remove organic pollutants effectively from contaminated effluent. Our results suggest that

cork is a useful adsorbent for the removal of all the phenolic compounds studied and especially for the more halogenated phenolic compounds, PCP and 2,4-DCP, which only require 24 and 54 $g.L^{-1}$ of cork, respectively, to reduce their concentrations from 1to 0.1 $mg.L^{-1}$.

- Cork was found to be an efficient sorbent for DCF, TCS, NAP, KET, CBZ and MPB. Only small amounts of cork, from 0.91 to 3.13 $g.L^{-1}$, were required to reduce the concentrations of NAP, KET, CBZ and MPB from 1 $mg.L^{-1}$ to 0.1 $mg.L^{-1}$. In the case of DCF and TCS, a 100% removal efficiency was obtained by using 5 mg of cork. PPCP sorption is not dependent on the amount of cork nor on the fact that some of these compounds are present in the solution in their ionized form at pH 6 since the adsorption process is based on the same π-π interactions.

GENERAL CONCLUSIONS:

- Microextraction techniques can be used to perform direct analyses using miniaturised equipment, achieving high enrichment factors that can allow the use of instrumentation available in non-specialised laboratories to be used, minimising solvent consumption and reducing waste and improving the performance in the analysis of complex water environmental samples. In this thesis, a simple, sensitive, effective and low-cost method, based on the combination of PDMS rod extraction with HPLC-DAD has been developed for the determination of four pharmaceutical compounds (NAP, KET, CBZ, DCF) and one ingredient of cosmetic products (TCS) in surface water samples.

- Adsorption is a less costly, simple and efficient alternative to advanced wastewater treatments for the removal of a variety of metallic and organic compounds from aqueous systems. Granulated cork can be used as a novel adsorbent of micropollutants, such as phenolic compounds and emerging contaminants. Its main advantages is that, unlike other adsorbents, no pre-treatment is required before use and, given that it is currently treated as a waste product within the industry, it can be acquired for little or no cost. The cork residue can be used in wastewater treatment plants located near cork production facilities resulting in reduced transportation costs.

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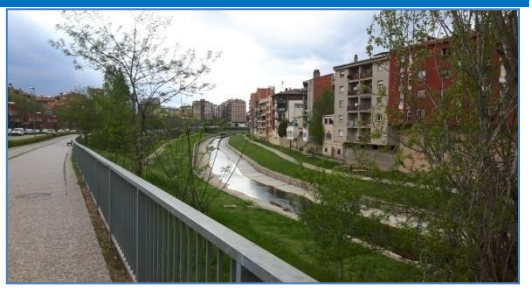

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