TESIS DOCTORAL

Programa de Doctorado en Química Fina

Diseño y aplicación de disolventes supramoleculares para el desarrollo de plataformas rápidas de tratamiento de muestra y detección

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Design and application of supramolecular solvents for the development of rapid sample treatment and detection platforms

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Doctoranda:

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Córdoba, Mayo de 2023

TITULO: *Diseño y aplicación de disolventes supramoleculares para el desarrollo de plataformas rápidas de tratamiento de muestra y detección*

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Tesis Doctoral

Diseño y aplicación de disolventes supramoleculares para el desarrollo de plataformas rápidas de tratamiento de muestra y detección

Trabajo presentado para aspirar al grado de Doctora, por

María Jesús Dueñas Mas

que lo firma en Córdoba, a 23 de mayo de 2023

Fdo. María Jesús Dueñas Mas

Graduada en Química

con el VºBº de las directoras,

Soledad Rubio Bravo y Ana Mª Ballesteros Gómez

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Ana Mª Ballesteros Gómez, Profesora Titular del Departamento de Química Analítica de la Universidad de Córdoba,

EN CALIDAD DE:

Directoras de la Tesis Doctoral titulada "*Diseño y aplicación de disolventes supramoleculares para el desarrollo de plataformas rápidas de tratamiento de muestra y detección*", presentada por MARÍA JESÚS DUEÑAS MAS, graduada en química,

CERTIFICAN:

1) Que el trabajo experimental de la Tesis Doctoral ha sido desarrollado en los laboratorios del Departamento de Química Analítica de la Universidad de Córdoba (España).
2) A su juicio, reúne todos los requisitos exigidos a este tipo de trabajos.

Y para que conste y surta los efectos pertinentes, expiden el presente certificado en Córdoba a 23 de mayo de 2023.

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Ana Mª Ballesteros Gómez, Associate professor of Analytical Chemistry of the University of Córdoba,

IN QUALITY OF:

Supervisors of the Doctoral Thesis entitled "*Design and application of supramolecular solvents for the development of rapid sample treatment and detection platforms*", presented by MARÍA JESÚS DUEÑAS MAS, graduated in chemistry,

CERTIFIES THAT:

1) The experimental work of the PhD thesis has been developed in the laboratories of the Department of Analytical Chemistry of the University of Córdoba (Spain).
2) According to their judgment, the thesis meets all the requirements of this type of scientific work.

Córdoba, 23rd May 2023.

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MENCIÓN DOCTORADO INTERNACIONAL

Mediante la defensa de esta Memoria de Tesis se opta a la obtención de la mención de "Doctorado Internacional" habida cuenta de que la doctoranda reúne los requisitos exigidos:

1. La doctoranda ha realizado una estancia de tres meses en la Universidad Vrije de Ámsterdam (Países Bajos) bajo la supervisión del prof. Dr. Jacob de Boer, donde ha desarrollado una de las investigaciones que constituyen esta Tesis.
2. Parte de esta Tesis Doctoral, en concreto los objetivos, el contenido y las conclusiones, se han redactado y serán presentadas en una de las lenguas oficiales de la Unión Europea distinta a cualquiera de las lenguas oficiales en España.
3. La Tesis cuenta con informes favorables de dos expertos doctores pertenecientes a instituciones de educación superior no españolas.
4. Uno de los miembros del tribunal evaluador de la Tesis es un experto doctor perteneciente a una institución de educación superior no española.

TÍTULO DE LA TESIS: Diseño y aplicación de disolventes supramoleculares para el desarrollo de plataformas rápidas de tratamiento de muestra y detección

DOCTORANDA: María Jesús Dueñas Mas.

INFORME RAZONADO DE LAS DIRECTORAS DE LA TESIS

La temática de la presente Tesis Doctoral ha estado enfocada en la síntesis y aplicación de disolventes supramoleculares (SUPRASs) para la extracción de compuestos en matrices complejas, como los alimentos, sus envases o el polvo doméstico. Se demuestra así la versatilidad de los SUPRASs para su uso como agentes extractantes en problemas analíticos.

Los compuestos en estudio han sido contaminantes emergentes, los cuales se consideran de especial interés debido a su ubicuidad, toxicidad y en ocasiones, falta de legislación sobre su presencia en determinados materiales, como por ejemplo en los envases en contacto con alimentos.

Las técnicas analíticas utilizadas durante el desarrollo de las investigaciones presentadas en esta Tesis Doctoral han sido, por un lado, cromatografía líquida acoplada a espectrometría de masas de baja y alta resolución, y por otro lado, la modalidad de espectrometría de masas ambiental, cuyo interés está creciendo debido a su rapidez de análisis y su facilidad de uso. Todo esto ha

permitido a la doctoranda adquirir una formación sólida en técnicas punteras y de gran relevancia.

Los resultados obtenidos mostraron la presencia de diversos contaminantes emergentes en las distintas matrices estudiadas, lo que supone un riesgo para la salud y para el medio ambiente.

Todo ello ha dado lugar a 7 artículos científicos publicados en revistas indexadas, todas ellas situadas en el primer cuartil (6 en JCR con dos de ellas del primer decil de su área y 1 en SJR también del primer decil). La doctoranda también es coautora de 1 capítulo de libro, otro artículo científico, un artículo de divulgación científica y una patente. Además, ha hecho contribuciones en 12 congresos científicos (5 internacionales y 7 nacionales) con 5 comunicaciones orales (tres de ellas internacionales) y 9 pósteres.

La estancia realizada en el grupo del profesor Jacob de Boer (Universidad Vrije de Ámsterdam, Países Bajos) supuso para la doctoranda una formación complementaria de otras técnicas de extracción y modos de trabajo, mejorando y ampliando sus conocimientos en el ámbito analítico.

Por todo ello, y en base a la originalidad de las investigaciones desarrolladas y presentadas en esta Memoria de Tesis, así como la formación científica adquirida por Dª. María Jesús Dueñas Mas, se autoriza la presentación de esta Tesis Doctoral.

En Córdoba, a 23 de mayo de 2023

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Profesora Titular del Departamento de Química Analítica de la Universidad de Córdoba

INFORME SOBRE LOS INDICIOS DE CALIDAD DE LA TESIS

A continuación, se detallan las publicaciones que se aportan como indicios de calidad de esta Tesis Doctoral.

1. **Supramolecular solvent-based microextraction of emerging bisphenol A replacements (colour developers) in indoor dust from public environments**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Chemosphere 222 (2019) 22-28.
- Índice de impacto de la revista: 5.778 (JCR 2019).
- Área temática: Environmental Sciences.
- Posición revista/nº total de revistas: 29/265 (Q1).

2. **Emerging bisphenol a replacements (colour developers) in indoor dust from Spain**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Emerging Contaminants 5 (2019) 168-172.
- Índice de impacto de la revista: 1.993 (SJR 2019).
- Área temática: Health, Toxicology and Mutagenesis
- Posición revista/nº total de revistas: 8/135 (D1).

3. **Supramolecular solvent-based microextraction of aryl-phosphate flame retardants in indoor dust from houses and education buildings in Spain**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Science of the Total Environment 733 (2020) 139291.
- Índice de impacto de la revista: 7.963 (JCR 2020).
- Área temática: Environmental Sciences.
- Posición revista/nº total de revistas: 25/274 (D1).

4. **Characterization of a new sustainable supramolecular solvent and application to the determination of oxy-PAHs in meat, seafood and fish tissues**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Food Chemistry 405 (2023) 134731.
- Índice de impacto de la revista: 9.231 (JCR 2021).
- Área temática: Chemistry, applied.
- Posición revista/nº total de revistas: 6/73 (D1).

5. **Supramolecular solvent-based microextraction probe for fast detection of bisphenols by ambient mass spectrometry**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Chemosphere 294 (2022) 133719.
- Índice de impacto de la revista: 8.943 (JCR 2021).
- Área temática: Environmental Sciences.
- Posición revista/nº total de revistas: 33/279 (Q1).

6. **Supramolecular solvent extraction and ambient mass spectrometry for the determination of organic contaminants in food packaging material**
- Autores: María Jesús Dueñas-Mas, Cristina de Dios-Pérez, Ana María Ballesteros-Gómez, Soledad Rubio.
- Revista: Chemosphere 324 (2023) 138359.
- Índice de impacto de la revista: 8.943 (JCR 2021).
- Área temática: Environmental Sciences.
- Posición revista/nº total de revistas: 33/279 (Q1).

7. **Determination of several groups of PFAS in food packaging material from different fast-food restaurants in France**
- Autores: María Jesús Dueñas-Mas, Ana María Ballesteros-Gómez, Jacob de Boer.
- Enviado a revista (Chemosphere).
- Área temática: Environmental Sciences.

Agradecimientos

Agradezco al Ministerio de Ciencias, Innovación y Universidades la concesión de una beca para la formación de doctores del programa nacional de Formación de Personal Investigador, con referencia PRE2018/083336, que me ha facilitado la plena dedicación a esta Tesis Doctoral, así como la realización de una estancia de tres meses en la Universidad Vrije de Ámsterdam.

Agradezco también a mis compañeros de grupo, que me han acompañado a lo largo de este recorrido, desde los primeros que estuvieron al inicio: *Noelia*, *Salatti*, *Franchesca*, *Encarni* y *Sole*; la gente que vino de estancia: *Laura Sofía*, *Manuela*, *Melisa*, *Nadir* y *Zainab*; y los que me acompañan ahora: *Lourdes*, *Luis*, *Celia*, *Nouman*, *Cristina* y *Loles* (y mi *Solete*, que continúa conmigo y ha sido mi sister de doctorando desde el principio), y también a mis compis de otros grupos y de cervezas de los viernes: *Paco*, *Juan*, *Laura*, ...

A *Lola* y *Loreto*, por sus enseñanzas y consejos. A *Lola* como jefa de Departamento, por las oportunidades que me ha dado. A *Juan Manuel*, por su paciencia y dedicación para adentrarme en la docencia. A *Laura Soriano*, por darme la oportunidad de hacer mis primeros pinitos publicando, sus enseñanzas en el TFG, y luego más tarde como compañera docente. Y a mis supervisoras *Soledad* y *Ana*, por todo lo que me han enseñado y el tiempo que me han dedicado. Sin vosotras realmente esto no hubiera sido posible; GRACIAS por haberme dado la oportunidad de formar parte del grupo.

A mi familia, porque sin su apoyo no hubiera llegado hasta donde estoy. A *mis padres* que son mi pilar fundamental, que han dado todo para que hoy este aquí, consiguiendo mis metas. A *mis hermanas*, por sus consejos y apoyo, y *mis cuñados* y *sobrinos*. GRACIAS de corazón por acompañarme en todo momento.

A mi compañero de vida, *Jonathan*. Que siempre está a mi lado a pesar de mis malos días, que no han sido pocos. GRACIAS por estar ahí, mi otro pilar fundamental.

Y por último, pero no menos importante, a *mis amigos*, a los de siempre. Los que consiguen que por un ratito se me olviden las penas y todo sean alegrías.

Índice

1.

Objetivos

En la actualidad existen multitud de compuestos químicos con efectos adversos para la salud y/o el medioambiente que son utilizados en una gran variedad de productos de consumo. Estos contaminantes se liberan fácilmente al medio ambiente o a los alimentos desde los envases que los contienen. El estudio de la exposición humana a los contaminantes resulta de gran relevancia, con el fin de identificar sus riesgos, fuentes de exposición, etc.

En este ámbito, ha surgido la necesidad de desarrollar nuevos métodos de tratamiento de muestra que sean más rápidos, económicos, fáciles de implementar y respetuosos con el medio ambiente. Además, dada la compleja contaminación presente en las muestras, deben de abarcar una gran variedad de grupos de compuestos sin comprometer su sensibilidad y selectividad.

Las investigaciones realizadas en esta Tesis pretenden contribuir a estos objetivos mediante el uso de disolventes supramoleculares (SUPRASs), cuyas propiedades y características permiten la extracción cuantitativa de compuestos y el desarrollo de métodos de tratamiento de muestras que cumplan los requisitos mencionados anteriormente. Las metodologías desarrolladas se acoplaron a cromatografía de líquidos y espectrometría de masas de baja y alta resolución, dada la versatilidad y alto poder de identificación de compuestos de estas técnicas. Además, se estudió la compatibilidad de los SUPRAS con espectrometría de masas ambiental (AMS, de sus siglas en inglés *Ambient Mass Spectrometry*) para un análisis ultra-rápido. La Tesis se divide en dos Bloques cuyos objetivos se desarrollan a continuación.

1.1. Bloque I: Desarrollo de estrategias analíticas para la determinación de contaminantes emergentes.

El objetivo principal del Bloque I de esta Tesis ha consistido en el desarrollo de tratamientos de muestra genéricos y rápidos basados en el uso de SUPRASs para la determinación y cuantificación de contaminantes emergentes (*ECs*, de sus siglas en inglés *Emerging Contaminants*) en muestras complejas (polvo doméstico, papel térmico, alimentos y envases) consideradas fuentes de exposición para los humanos. Los objetivos específicos del Bloque I fueron los siguientes:

1. Investigación del potencial de los SUPRASs con propiedades de acceso restringido, constituidos por agregados hexagonales inversos de 1-hexanol, en mezclas de tetrahidrofurano (THF) y agua, para el desarrollo de tratamientos de muestra innovadores y en una sola etapa para la determinación de ECs en muestras sólidas de interés mediante LC-MS.

2. Desarrollo de un SUPRAS sostenible con propiedades de acceso restringido, sintetizado con 1-hexanol y 2-metiltetrahidrofurano o 2-

MeTHF (que es un disolvente obtenido de biomasa vegetal) que sustituye al THF en el medio hidroorgánico requerido para la coacervación. Aplicación del nuevo SUPRAS para la extracción de ECs en muestras sólidas que suponen un riesgo para la exposición humana.

3. Focalizar la investigación en ECs y fuentes de exposición de los cuales se necesita información acerca de su presencia y su distribución. Los métodos basados en SUPRASs-LC-MS fueron desarrollados y validados para: (a) bisfenol A (BPA) y sus compuestos sustituyentes (bisfenol S o BPS, bisfenol F o BPF, 4-(4-fenilmetoxifenilo) sulfonilfenol o BPS-MAE, 4-(4-propan-2-iloxifenilo) sulfonilfenol o D8 y 4-(4-hidroxi-3-prop-2-enilfenilo) sulfonil-2-prop-2-enilfenol o TGSA) en muestras de polvo de hogares, tiendas, restaurantes y coches. (b) Retardantes de llama organofosforados con sustituyentes arilo (*aryl-OPFRs,* de sus siglas en inglés *Aryl-Organophosphate Flame Retardants*), como bisfenol A bis(difenil fosfato) o BDP, cresil difenil fosfato o CDP, 2-etilhexil difenil fosfato o EHDPP, isodecil difenil fosfato o IDPP, resorcinol bis(difenil fosfato) o RDP, y trifenil fosfato o TPHP en muestras de polvo de hogares y centros educativos. (c) Hidrocarburos policíclicos aromáticos oxigenados (*oxy-PAHs*, de sus siglas en inglés *oxygenated polycyclic aromatic hydrocarbons*) en comida procesada.

4. Estudio de las diferencias en la presencia de los contaminantes en polvo entre distintos microambientes, de las correlaciones entre dichos compuestos y de la exposición humana por ingestión (vía oral) en adultos y niños.

5. Estudio de la presencia y niveles de concentración de oxy-PAHs en comidas procesadas (fritas, ahumadas, etc.).

6. Adquisición de experiencia por parte de la doctoranda mediante la determinación de otros ECs durante su estancia en un centro de investigación extranjero con una destacada experiencia en el área.

1.2. Bloque II: Combinación de los SUPRASs con espectrometría de masas ambiental y aplicaciones.

El objetivo principal del Bloque II de esta Tesis ha sido el estudio del acoplamiento de un tratamiento genérico de muestra con SUPRASs con AMS con el fin de desarrollar métodos rápidos de cribado que puedan aplicarse a matrices complejas. Los objetivos específicos del Bloque II son los siguientes:

1. Investigación del potencial como extractantes de los SUPRASs introducidos en un capilar de vidrio (sonda) y su compatibilidad con la técnica AMS ASAP (de sus siglas en inglés *Atmospheric Solids Analysis Probe*) por primera vez.

2. Aplicación del método desarrollado: (a) al estudio de la presencia de diferentes sustitutos del BPA en tickets de la compra de diferentes establecimientos, donde son normalmente usados, y (b) a la cuantificación de sustitutos del BPA y ayl-OPFRs en envases de alimentos plásticos, usando AMS de baja resolución.

3. Aplicación de los métodos desarrollados al cribado basado en una búsqueda con librería espectral con espectrometría de masas de alta resolución para el análisis de envases de alimentos.

Con el desarrollo de esta Tesis se pretende que la doctoranda adquiera las competencias y habilidades que se recogen en el Reglamento del Programa de Doctorado de Química Fina, además de servir como aportación en el avance de la investigación. Entre dichas competencias y habilidades se encuentran:

- La capacidad de diseñar un proceso de investigación de cierta complejidad y relevancia, mediante el diseño de los experimentos y su realización de forma autónoma.

- La capacidad de realizar análisis crítico de los resultados obtenidos, así como de su discusión.
- La capacidad de comunicación de los resultados mediante la redacción de artículos científicos y la exposición en congresos.

1.

Objectives

Currently, there are a huge number of chemical compounds with adverse effects to the human health and the environment, which are used in a wide variety of products. These compounds are easily released to the environment or to the food from food-contact materials. The study of human exposure to contaminants is of great relevance in order to identify their risk, exposure sources, etc.

Another goal is the necessity to develop new sample-treatment methods, which are more economic, faster, easier to implement, more eco-friendly and suitable for a wide variety of matrices and analytes.

The research from this Thesis intends to contribute to both objectives through the use of supramolecular solvents (SUPRASs), whose characteristics and properties allow the quantitative extraction of compounds and the development of sample treatment methods which fulfil the requirements above mentioned. The developed methodologies were coupled to liquid chromatography and low and high-resolution mass spectrometry, because of their versatility and high potential for the

identification of compounds. In addition, SUPRASs compatibility with ambient mass spectrometry (AMS) was studied for ultra-fast analysis for the first time. This Thesis is divided in two Blocks whose objectives are explained below.

1.1. Block I: Development of analytical strategies for the determination of emerging contaminants.

The main objective of Block I was the development of fast and generic sample treatments based on the use of SUPRASs for the determination and quantification of emerging contaminants (ECs) in complex matrices considered as exposure sources for humans (indoor dust, thermal paper, food and food contact materials). Specific objectives of Block I were the following:

1. To investigate the potential of SUPRASs with restricted access properties, made up of hexagonal reversed aggregates of 1-hexanol, in mixtures of tetrahydrofuran (THF) and water, for the development of innovative single-step sample treatments in the determination of ECs in solid samples of interest for human exposure by LC-MS.

2. To develop greener SUPRASs with restricted access properties, based on 1-hexanol, by replacing THF by 2-methyl-tetrahydrofuran (a solvent obtained from plant biomass) in the hydro-organic medium required for coacervation. Application of the new SUPRASs to the extraction of ECs from solid samples that constitute a risk to the human exposure.

3. To focus the investigation on ECs and exposure sources for which new data on occurrence and distribution is required. In this respect, methods based on SUPRAS-LC-MS are developed and validated for: (a) bisphenol A (BPA) and its substituents (bisphenol S or BPS, bisphenol F or BPF, 4-(4-phenylmetoxyphenyl) sulfonylphenol or BPS-MAE, 4-(4-propan-2-yloxyphenyl) sulfonylphenol or D8 and 4-(4-hydroxy-3-prop-2-

enylphenyl) sulfonyl-2-prop-2-enylphenol or TGSA) in dust from homes, shops, restaurants and cars. (b) Aryl-organophosphate flame retardants (aryl-OPFRs), such as bisphenol A bis(diphenyl phosphate) or BDP, cresyl diphenyl phosphate or CDP, 2-ethylhexyl diphenyl phosphate or EHDPP, isodecyl diphenyl phosphate or IDPP, resorcinol bis(diphenyl phosphate) or RDP, and triphenyl phosphate or TPHP in domestic and schools dust. (c) Oxygenated Polycyclic Aromatic Hydrocarbons (oxy-PAHs) in processed foods.

4. To study the differences in the presence of contaminants in dust between different microenvironments, the correlations between the target compounds, and the human exposure by ingestion (oral route) in adults and children.

5. To study the occurrence and concentration levels of oxy-PAHs in fried and smoked food.

6. To get experience about the determination of other ECs by the stay that the PhD student performed abroad in a research center with large expertise in this area.

1.2. Block II: Combination of SUPRAS and ambient mass spectrometry and applications.

The main objective of Block II was to study the coupling of a generic sample treatment (based on SUPRASs) with AMS, with the aim of developing faster screening methods which can be applied to complex matrices. Specific objectives of Block II were the following:

1. To investigate de potential as extractant of SUPRASs introduced into a glass capillary (probe) and their compatibility with AMS ASAP (Atmospheric Solids Analysis Probe) technique for the first time.

2. To apply the developed extraction method: (a) to the study of the presence of different BPA substituents in purchase receipts from different establishments, where they are usually used, and (b) to quantify BPA substituents and aryl-OPFRs in plastic food packaging, using low-resolution AMS.

3. Application of the developed methods to a wide screening based on a mass spectral library search with high-resolution MS in food packaging.

The development of this Thesis pursues that the student acquires the competences and skills set out in the Regulations of the Doctoral Program in Fine Chemistry, in addition to be a contribution to research. Some of these competences and skills are:

- Capacity of design a research process with certain complexity and relevance through the design of experiments and their performance.
- Capacity of perform critical analysis of results and their discussion.
- Capacity to communicate the results by the redaction of scientific papers and their exposition in congresses.

2.

Contenido

La memoria de esta Tesis Doctoral se ha estructurado en varias secciones. En primer lugar, se expone la Introducción, donde se describen los diferentes grupos de contaminantes estudiados, así como las distintas matrices que se han investigado. También se describen aspectos teóricos y prácticos de los disolventes supramoleculares (SUPRASs), y, finalmente, se discute la técnica de espectrometría de masas ambiental (AMS, de sus siglas en inglés *Ambient Mass Spectrometry*).

A continuación, se exponen los contenidos de los Bloques I y II, donde se describen los distintos Capítulos que se corresponden con los artículos científicos derivados de las investigaciones realizadas.

Finalmente, se exponen las conclusiones más relevantes de los distintos estudios, seguidas de los Anexos donde se recogen otras publicaciones científicas y de divulgación, así como las comunicaciones presentadas en congresos científicos.

Bloque I: Desarrollo de estrategias analíticas para la determinación de contaminantes emergentes.

En este Bloque se han recogido los Capítulos I – V, relacionados con el uso de los SUPRASs para la determinación y cuantificación de contaminantes emergentes (ECs). En el Capítulo I se ha desarrollado un método de extracción del Bisfenol A (BPA) y sus compuestos análogos basado en SUPRASs de agregados inversos de 1-hexanol en mezclas de tetrahidrofurano (THF) y agua, siendo la matriz estudiada el polvo doméstico de distintos lugares públicos (tiendas, restaurantes, etc.). En el Capítulo II se aplicó el método desarrollado anteriormente al mismo grupo de compuestos en muestras de polvo de casas, coches y oficinas, con el fin de realizar estudios estadísticos para poner de manifiesto las diferencias de contaminación entre dichos microambientes y calcular el nivel de exposición humana, mientras que en el Capítulo III se aplicó el mismo método a retardantes de llama organofosforados para estudiar su presencia en polvo doméstico de hogares y centros escolares (guarderías, colegios, universidad, etc.), así como calcular el nivel de exposición humana de las personas que trabajan/estudian en dichos lugares. Por otro lado, en el Capítulo IV, se ha desarrollado y caracterizado un nuevo SUPRAS basado también en agregados inversos de 1-hexanol para la extracción de contaminantes orgánicos, pero sustituyendo el THF por un disolvente verde (2-metil-tetrahidrofurano o 2-MeTHF).Como prueba de concepto se aplicó a la extracción de hidrocarburos policíclicos aromáticos oxigenados (oxy-PAH) en muestras de alimentos cocinados (pescado, marisco y carne). Estos compuestos han sido hasta la fecha escasamente estudiados en alimentos. Por último, en el Capítulo V se ha estudiado la presencia de sustancias per y polifluoroalquiladas (PFAS) en envases de alimentos, ya que son un grupo de compuestos utilizados para su síntesis con el fin de proteger el material del que están hechos (normalmente papel o cartón) de la humedad y oleosidad del alimento que contienen. Este último estudio se llevó a cabo en la estancia realizada por la doctoranda en

la Vrije Universidad de Amsterdam bajo la supervisión de prof. Jacob de Boer.

Bloque II: Combinación de los SUPRASs con espectrometría de masas ambiental y aplicaciones.

En este bloque se recogen los Capítulos VI y VII donde se ha estudiado el uso de los SUPRASs con la técnica de AMS de tipo ASAP (*de sus siglas en inglés Atmospheric Solid Analysis Probe*) para estudiar, por un lado, el BPA y sus compuestos análogos en papel térmico (Capítulo VI), y por otro, determinar y cuantificar dicho grupo de compuestos junto con retardantes de llama organofosforados en envases de alimentos (Capítulo VII). En este último capítulo también se hace un cribado de compuestos sospechosos mediante búsqueda en librería espectral en las muestras de envases mediante el uso de espectrometría de masas ambiental de alta resolución.

2.

Summary

This Doctoral Thesis has been structured in several sections. Firstly, in the *Introduction* the different studied groups of contaminants and the investigated matrices are discussed. Then, theorical and practical aspects of supramolecular solvents (SUPRASs) are described, and finally, the emerging technique of ambient mass spectrometry (AMS), used in some studies of this Thesis, is presented.

Secondly, Blocks I and II are exposed, composed by the different chapters which correspond to the scientific articles derived from the performed research in this Thesis.

Finally, the most relevant conclusions from the different studies are exposed, followed by the Annexes which contain other scientific and divulgation publications, as well as the communications presented in scientific congresses.

Block I: Development of analytical strategies for the determination of emerging contaminants.

In this block, Chapters I – V are discussed, related with the use of SUPRASs for the determination and quantification of emerging contaminants (ECs). In Chapter I, an extraction method of bisphenol A (BPA) and its replacements based on SUPRASs has been developed, being indoor dust from different public establishments the studied matrix. In Chapter II, the developed method was applied to the analysis of same group of compounds in dust samples from houses, indoor cars and offices. Statistical studies about the differences in contamination between microenvironments and about the possible correlations between the levels of different contaminants were carried out. In Chapter III, the same method as in Chapter I was also applied to the determination of organophosphate flame retardants (aryl-OPFRs) in dust from houses and education buildings (kindergartens, schools, universities, etc.). In addition, human exposition via indoor dust ingestion was calculated to investigate the exposition of people who work/study in these places (this was also calculated in Chapter II). On the other hand, in Chapter IV, a new SUPRASs has been developed and characterized formed by fatty alcohols and a green solvent (2-methyl-tetrahydrofuran, 2-MeTHF) instead of THF, which has been used for the extraction of polycyclic aromatic hydrocarbons (oxy-PAHs) in cooked food samples (fish, sellfish and meat). The presence of these emerging contaminants in food has been scarcely investigated. Finally, in Chapter V, per- and polyfluoroalkyl substances (PFAS) have been studied in food packaging materials, due to the fact that they are compounds used in their synthesis with the aim of protecting the material (usually made of paper or cardboard) from the moisture and grease of the contained food. This last study is a result of the research carried out by the PhD candidate at the short stay performed at the Vrije University of Amsterdam under the supervision of prof. Jacob de Boer.

Block II: Combination of SUPRASs and ambient mass spectrometry and applications.

In this block, Chapters VI and VII are exposed, where the use of SUPRASs with the AMS technique ASAP (Atmospheric Solid Analysis Probe) has been investigated to study BPA and its replacements in thermal paper (Chapter VI), and to determine and quantify this group of contaminants together with organophosphate flame retardants in food packaging materials (Chapter VII). In this chapter, a wide screening of suspect compounds is also carried out, based on a mass spectral library search with high-resolution AMS in food packaging.

3.

Introducción

3.1. Contaminantes emergentes

Los contaminantes ambientales pueden clasificarse en prioritarios y emergentes. Los prioritarios incluyen aquellos regulados (sometidos a un régimen de control de emisiones y/o monitoreo de rutina), como los pertinentes a la calidad del aire (2008/50/EC), del agua (2000/60/EC) o los alimentos (1881/2006 CE). Los contaminantes emergentes (*ECs*, de sus siglas en inglés *Emerging Contaminants*) abarcan una gran variedad de grupos de compuestos, incluyendo sus metabolitos y productos de transformación, que han sido determinados recientemente (o incluso cuantificados) [1]. Aún no tienen directrices ni legislación pertinente, pero suponen un riesgo para la salud y el medioambiente y suelen estar bajo escrutinio para futuras regulaciones. Estos compuestos no son necesariamente de reciente desarrollo industrial, de hecho, la mayoría son sustancias que han contaminado al medioambiente durante años, incluso décadas, pero su presencia sólo ha comenzado a investigarse recientemente gracias a los avances que se han producido en las metodologías analíticas. Entre los contaminantes emergentes

encontramos compuestos industriales, productos farmacéuticos, productos cosméticos y productos fitosanitarios, entre otros [2]. La lista de compuestos crece constantemente, lo que no es sorprendente si tenemos en cuenta que actualmente hay más de 100 millones de sustancias químicas registradas y que alrededor de 4.000 nuevos CAS se registran cada día [3]. La red NORMAN (https://www.norman-network.net/), una red permanente de laboratorios de referencia y organizaciones relacionadas que se ocupan de sustancias ambientales emergentes [3], compila los principales CE, proporcionando bases de datos de carácter abierto y fomentando la armonización de protocolos y la mejora de la calidad de los datos sobre los mismos.

Es sabido que muchos de estos contaminantes tienen capacidad de migración, son persistentes en el medio ambiente y tóxicos incluso a bajas concentraciones [4]. Debido a esto, existe una creciente preocupación con respecto a la exposición humana y el medio ambiente, y sus posibles efectos adversos a corto y largo plazo [2]. Dicha exposición puede darse a través de diferentes vías, como la inhalación, la ingestión o la absorción directa a través de la piel. Por ello, resulta de gran relevancia el estudio de matrices que constituyan vías mayoritarias de exposición como el polvo doméstico, los alimentos y sus envases, o el papel térmico, un material frecuentemente utilizado como por ejemplo en los tickets de la compra.

En esta Tesis nos centramos en evaluar varias familias de contaminantes emergentes como los bisfenoles (bisfenol A y sus compuestos análogos) y retardantes de llama organofosforados con sustituyente arilo en muestras de polvo doméstico y envases de alimentos, así como hidrocarburos policíclicos aromáticos oxigenados en alimentos cocinados y sustancias per- y polifluoradas en envases de alimentos. Los bisfenoles también han sido estudiados en papel térmico, donde su uso es frecuente como sustitutos del bisfenol A.

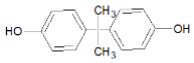
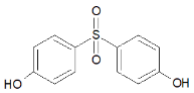
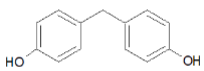
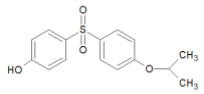
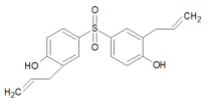
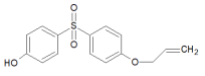
3.1.1. Bisfenol A y compuestos análogos

El bisfenol A (BPA) es un compuesto usado principalmente como monómero para la síntesis de resinas epoxi y policarbonatos, usados para el recubrimiento de latas de comida y para la fabricación de botellas reusables, biberones, o recipientes plásticos, respectivamente [5]. Otros usos del BPA son como aditivo en plásticos como el PVC (por ejemplo, para material médico), en pinturas y tintas de impresora, adhesivos o en papel térmico usado en tickets de la compra como revelador del color [6,7]. Debido a su extendido uso y su capacidad de migración (ya que puede quedar como monómero residual sin polimerizar en el plástico, o liberarse tras la hidrólisis de los enlaces que lo retienen debido al calor o la acidez o basicidad del contenido de los envases [8]), se encuentra de manera generalizada en el medio ambiente. Por ejemplo, ha sido encontrado en sedimentos (6,1 – 30,4 ng·g^{-1} [9], 2,2 – 16,7 ng·g^{-1} [10] , 3,1 – 25,8 ng·g^{-1} [11] y 0,6 – 10,6 ng·g^{-1} [12]), en aguas de ríos (10,8 – 45,3 ng·L^{-1} [9], 410 – 5.190 ng·L^{-1} [12] y 118 – 1.770 ng·L^{-1} [13]) y de mar (3,3 – 49,5 ng·L^{-1} [9], 2,3 – 49 ng·L^{-1} [14], 13.000 – 15.000 ng·L^{-1} [15] y 6 – 407 ng·L^{-1} [16]), en aire (0,1 – 2,5 ng · m^{-3}), polvo doméstico (860 – 9.726 ng·g^{-1} [17], 200 – 7.200 ng·g^{-1} [18] y 540 – 26.200 ng·g^{-1} [19]); y también en muestras biológicas como orina (<LOQ – 590 ng·L^{-1} [20] y <LOD – 740 ng·L^{-1} [21]), saliva (150 – 3.640 ng·L^{-1} [22], 57 – 800 ng·L^{-1}[23] y 15.300 – 32.400 ng·L^{-1} [24]) o sangre (<LOQ – 1.650 ng·L^{-1} [20] y 3.700 – 82.600 ng·L^{-1} [21]).

El BPA actúa como disruptor endocrino afectando a la hormona tiroidea, lo que influye en el desarrollo de los vertebrados [25,26], además de afectar también a nivel neuronal, metabólico, cardiovascular e inmunológico [27]. Con el fin de proteger la salud humana, su uso ha sido regulado, estableciendo la Directiva UE No. 2018/213 un límite máximo de migración del BPA (del envase al alimento) de 0.05 mg·kg^{-1} y un límite máximo de ingestión de 4 μg·kg^{-1} de peso al día [28]. También se ha prohibido su uso en materiales de uso infantil como biberones (EU Commission Directive No. 8/2011). Es por ello que la industria ha comenzado a introducir compuestos análogos con el fin de sustituirlo, como

por ejemplo el bisfenol S (BPS) o el bisfenol F (BPF), y otros menos conocidos como 4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (conocido como TGSA), 4-(4-phenylmethoxyphenyl) sulfonylphenol (BPS-MAE), 4-(4-propan-2-yloxyphenyl)sulfonylphenol (D8), etc. En la Tabla 1 se muestran los compuestos estudiados en esta Tesis, junto con su CAS, estructura molecular y fórmula.

Tabla 1. Nombre, CAS, estructura molecular y fórmula del BPA, BPS, BPF, D-8, TGSA y BPS-MAE.

Compuesto & CAS	Estructura molecular	Fórmula
4,4'-(propano-2,2-diil) difenol (BPA) ***80-05-7***		$C_{15}H_{16}O_2$
4,4'-Sulfonildifenol (BPS) ***80-09-1***		$C_{12}H_{10}O_4$
4,4'-Metilenodifenol (BPF) ***620-92-8***		$C_{13}H_{12}O_2$
4-(4-propan-2-iloxifenyl) sulfonilfenol (D-8) ***95235-30-6***		$C_{15}H_{16}O_4S$
4-(4-hidroxi-3-prop-2-enilfenyl)sulfonil-2-prop-2-enilfenol (TGSA) ***41481-66-7***		$C_{18}H_{18}O_4S$
4-(4-fenylmetoxifenil) sulfonilfenol (BPS-MAE) ***63134-33-8***		$C_{19}H_{16}O_4S$

Sin embargo, estos compuestos emergentes no han sido estudiados en profundidad (solo existen estudios de algunos como el BPS y el BPF [29–31]), por lo que todavía existe mucha desinformación acerca de sus efectos a corto y largo plazo en los humanos y en el medio ambiente, y debido a que son estructuralmente análogos al BPA, se espera que actúen de forma similar a nivel fisiológico, causando efectos parecidos [32].

En la presente Tesis, algunos de estos análogos han sido determinados por primera vez en muestras de polvo de casas, coches, oficinas y establecimientos públicos (*capítulos I y II*) y en papel térmico [33]. Los bisfenoles más ubicuos en estas matrices son el BPA y el BPS (y también BPF en el caso del polvo doméstico). En el estudio más reciente sobre papel térmico, el BPS fue el bisfenol predominante (61% de las muestras, como veremos en el *capítulo VI*), resultado que está en acorde con la nueva legislación ECHA/NR/20/22 que restringe el uso de BPA en estos artículos [34]. La presencia de estos compuestos análogos en polvo muestra su capacidad de migración y persistencia, que unido al desconocimiento de su toxicidad y posibles efectos adversos, los convierte en objeto de preocupación. Por otro lado, los bisfenoles también han sido estudiados en envases de alimentos (*capítulo VII*), donde junto con otros compuestos determinados mediante cribado, suponen un riesgo para la salud humana debido a la exposición diaria a este tipo de materiales.

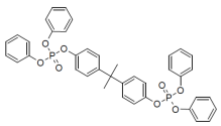
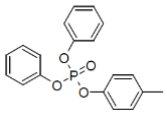
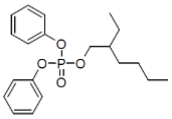
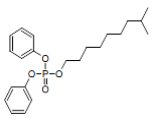
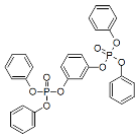
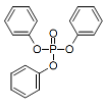
3.1.2. Retardantes de llama organofosforados con sustituyentes arilo (aryl-OPFRs)

Los retardantes de llama organofosforados con sustituyentes arilo (*aryl-OPFRs*, de sus siglas en ingles *Aryl-Organophosphate Flame Retardants*) pertenecen al grupo de compuestos de los retardantes de llama organofosforados (OPFRs) junto con los clorados (*chlorinated* OPFRs) y los

alquilados (*alkyl*-OPFRs) [35]. Los OPFRs son usados como alternativa a otros retardantes de llama (principalmente los éteres de difenilo polibromados, PBDEs, de sus siglas en inglés *Polybrominated Diphenyl Ethers*) [36], y como su propio nombre indica, son utilizados para hacer más resistentes a los materiales del fuego, siendo adicionados en una amplia variedad de productos, desde muebles y textiles domésticos (cortinas, alfombras, etc.) hasta equipos electrónicos, interiores de coches, pinturas, materiales de construcción, etc. [36]. También son usados como plastificantes en pulimentos para suelos, agentes antiespumantes, recubrimientos o resinas epoxi, entre otras aplicaciones [36,37]. Al tratarse de aditivos, son compuestos que tienen una alta capacidad de migración (bien por lixiviación o bien por volatilización o abrasión [38]), habiendo sido encontrados en diversas matrices como suelos (38 – 2.100 ng·g^{-1} [39], 2,4 – 36 ng·g^{-1} [40], 0,5 – 55 ng·g^{-1} [41] y 1,1 – 288 ng·g^{-1} [42]), sedimentos (3,8 – 824 ng·g^{-1} [43], 1,2 – 19 ng·g^{-1} [44] y 13,2 – 377 ng·g^{-1} [45]), lodos (97 – 1.310 ng·g^{-1} [46], 1.185 – 13.370 ng·g^{-1} [47] y 419 – 2.129 ng·g^{-1} [48]) agua (7,6 – 7.200 ng·L^{-1} [43], 36 – 469 ng·L^{-1} [49]y 150 – 885 ng·L^{-1} [44]), aire (13 – 420 ng· m^{-3} [50], 0,3 – 4,8 ng·m^{-3} [42] y 0,01 – 18 ng·m^{-3} [51]), polvo doméstico (5.822 – 148.215 ng·g^{-1} [50], 5.800 – 160.000 ng·g^{-1} [52] y 914 – 42.700 ng·g^{-1} [39]) y biota (300 – 1.900 ng·g^{-1} [53], 110 – 15.000 ng·g^{-1} [54] y 432 – 510 ng·g^{-1} [55]), entre otros.

También son potencialmente tóxicos (son carcinógenos, afectan a la reproducción, son disruptores endocrinos, neurotóxicos, etc. [36,37]), lo que hace que exista una especial preocupación por la exposición humana a estos compuestos, que puede darse por contacto dérmico o por inhalación o ingestión de partículas de polvo o comida contaminada. Es por ello que en la presente Tesis, los aryl-OPFRs han sido estudiados en dos matrices diferentes: polvo doméstico (*capítulo III*) y envases de alimentos (*capítulo VII*). En la Tabla 2 se muestran los nombres de los compuestos estudiados y su CAS, así como su estructura molecular y su fórmula.

Tabla 2. Nombre del compuesto y CAS, estructura molecular y fórmula de BDP, CDP, EHDPP, IDPP, RDP y TPHP.

Compuesto & CAS	Estructura molecular	Fórmula
Bisfenol A bis(difenil fosfato) (BDP) ***5945-33-5***		$C_{39}H_{34}O_8P_2$
Cresil difenil fosfato (CDP) ***26444-49-5***		$C_{19}H_{17}O_4P$
2-etilhexil difenil fosfato (EHDPP) ***1241-94-7***		$C_{20}H_{27}O_4P$
Isodecil difenil fosfato (IDPP) ***29761-21-5***		$C_{22}H_{31}O_4P$
Resorcinol bis(difenil fosfato) (RDP) ***57583-54-7***		$C_{30}H_{24}O_8P_2$
Trifenil fosfato (TPHP) ***115-86-6***		$C_{18}H_{15}O_4P$

A diferencia del BPA y sus análogos, no existen restricciones legislativas sobre el uso de estos compuestos. Algunos, como el BDP, TPHP o el RDP están incluidos en la lista certificada TCO (lista que garantiza que los equipos electrónicos no contienen sustancias que suponen un riesgo para la salud a largo plazo) como compuestos alternativos a otros retardantes de llama [56], siendo considerados menos tóxicos y no lo suficientemente peligrosos como para ser restringidos. Otros, como el EHDPP, están permitidos para su uso en materiales en contacto con alimentos (*FCMs*, de sus siglas en inglés *Food Contact Materials*), siendo el único de los mencionados en la Tabla 2. Sin embargo, hay estudios que demuestran la

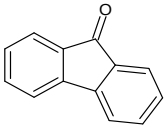
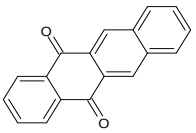
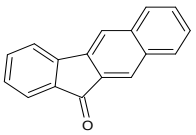
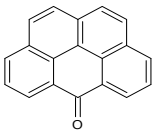
presencia de otros compuestos en envases de alimentos, como por ejemplo TPHP, que fue determinado en tetrabricks y envases de zumo junto con EHDPP [57]. Otro estudio, también encontró concentraciones en el intervalo de 0,26 – 0,82 $ng \cdot g^{-1}$ de TPHP en muestras alimentarias [58]. Estas investigaciones confirman la capacidad de migración que tienen estos compuestos, y por lo tanto, del riesgo que suponen para la salud humana y medioambiental.

3.1.3. Hidrocarburos policíclicos aromáticos oxigenados (oxy-PAHs)

Los hidrocarburos policíclicos aromáticos oxigenados (*oxy-PAHs*, de sus siglas en inglés *Oxygenated Polycyclic Aromatic Hydrocarbons*) son derivados del grupo de los hidrocarburos policíclicos aromáticos (PAHs) que contienen en su estructura uno o más átomos de oxígeno, que pueden provenir de los grupos funcionales cetona, lactona, quinona, carboxaldehído o ácido carboxílico [59]. Pueden originarse bien por la degradación biológica, química o enzimática de los PAHs [60] o bien por combustión incompleta del carbón, la materia orgánica o el aceite a temperaturas superiores a 500ºC [61]. Son compuestos altamente tóxicos, en ocasiones incluso más que los PAHs de los que proceden, actuando como disruptores endocrinos [62] y agentes mutagénicos [63]. Esta elevada toxicidad es debida a su potencial para mutar y a su biodisponibilidad [59], ya que al ser más polares son más solubles en agua y esto hace que tengan mayor movilidad en el ambiente. Por tanto, pueden migrar al agua superficial fácilmente donde posteriormente se evaporan a la atmósfera, o al agua subterránea donde su vida media es elevada [59]. Además, son contaminantes que no están legislados.

A pesar de que estos compuestos aparecen en los alimentos cuando son cocinados, no existen muchos estudios acerca de su presencia en los mismos, a diferencia de sus precursores los PAHs [64–66]. En esta Tesis se investiga la presencia de cuatro oxy-PAHs en alimentos procesados (pescados, mariscos y carnes) (*capítulo IV*). En la Tabla 3 se muestran los nombres de los compuestos estudiados, junto con su CAS, su estructura molecular y su fórmula, los cuales fueron seleccionados debido a que son compuestos prioritarios dada su toxicidad, y en el caso del primero (9H-fluoren-9-one) por ser un oxy-PAH analizado frecuentemente dada su ubicuidad.

Tabla 3. Nombre del compuesto y CAS, estructura molecular y fórmula de 9-Fluo, 5,12-Napht, 11-B(b)Fluo y 6-B(cd)Pyr.

Compuesto & CAS	Estructura molecular	Fórmula
9H-fluoren-9-ona (9-Fluo) ***486-25-9***		$C_{13}H_8O$
Naphtaceno-5,12-diona (5,12-Napht) ***1090-13-7***		$C_{18}H_{10}O_2$
11H-Benzo[b]fluoren-11-ona [11-B(b)Fluo] ***3074-03-1***		$C_{17}H_{10}O$
6H-Benzo[cd]piren-6-ona [6-B(cd)Pyr] ***3074-00-8***		$C_{19}H_{10}O$

3.1.4. Sustancias per- y poli-fluoroalquiladas (PFAS)

Las sustancias per- y polifluoroalquiladas (*PFAS*, de sus siglas en inglés *Per- and Polyfluoroalkylsubstances*) son un grupo de compuestos muy variado cuya cadena hidrocarbonada está total o parcialmente reemplazada por átomos de flúor, respectivamente [67]. Este enlace carbono-flúor es el enlace más resistente que existe [68,69], y hace que estos compuestos no se degraden, incluso a elevadas temperaturas, y que sean repelentes tanto al agua como al aceite al mismo tiempo [70]. Es por ello que han sido utilizados en una gran variedad de productos y aplicaciones desde 1940: pinturas, textiles, metales, pesticidas, utensilios de cocina, envoltorios de comida, etc. [71,72].

Debido a su ubicuidad, capacidad de migración y resistencia a la degradación, se consideran compuestos de elevada toxicidad. De hecho, existen numerosos estudios que los relacionan con diversos cánceres, inmunotoxicidad y problemas en el desarrollo [73]. Es por esto que algunos han sido regulados e incluso restringidos por las autoridades, como es el caso del ácido perfluorooctanoico (*PFOA*, de sus siglas en inglés *Perfluorooctanoic acid*), restringido desde el 4 de Julio del 2020 [74] o el ácido perfluorooctanosulfónico (*PFOS*, de sus siglas en inglés *Perfluorooctane sulphonic acid*) y sus sales, que han sido incluidos en el Anexo B del Convenio de Estocolmo como contaminantes orgánicos persistentes (*POPs*, de sus siglas en inglés *persistent organic pollutants*) [75]. Como alternativas, se han comenzado a usar PFAS de cadena más corta, como el ácido perfluorobutanoico (PFBA, de sus siglas en inglés *Perfluorobutanoic acid*), ácido perfluoropentanoico (*PFPeA*, de sus siglas en inglés *Perfluoropentanoic acid*) y ácido perfluorohexanoico (*PFHxA*, de sus siglas en inglés *Perfluorohexanoic acid*) [71], ya que se ha demostrado que su vida media en el organismo es más corta [76]. Sin embargo, son compuestos que tienen mayor movilidad debido a su solubilidad en agua y elevada volatilidad, por lo que son incluso más ubicuos que los de cadena más larga [69,77].

Uno de los principales usos de los PFAS siempre ha sido como protector de los envases de alimentos (especialmente los de papel y cartón), con el fin de evitar que se impregnen y/o rompan debido al contenido graso y/o acuoso del alimento que contienen. Debido a su capacidad de migración al alimento (como han demostrado numerosas investigaciones[71,78–80]) y su toxicidad, el estudio sobre su presencia en FCMs está en auge, especialmente con el fin de poder prohibir su uso por completo, o por lo menos, reducir al máximo su presencia.

En la Tabla 4 se muestran los PFAS más relevantes estudiados en esta Tesis (*capítulo V*), junto con su abreviatura y su CAS.

Tabla 4. Nombre del compuesto, abreviatura y CAS.

Compuesto	Abreviatura	CAS
Ácido Perfluorobutanoico	PFBA	375-22-4
Ácido Perfluoropentanoico	PFPeA	2706-90-3
Ácido Perfluorohexanoico	PFHxA	307-24-4
Ácido Perfluoroheptanoico	PFHpA	375-85-9
Ácido Perfluorooctanoico (lineal)	PFOA	335-67-1
Ácido Perfluorooctanoico (ramificado)	PFOA Br	335-67-1
Ácido Perfluorononanoico	PFNA	375-95-1
Ácido Perfluorodecanoico	PFDA	335-76-2
Ácido Perfluoroundecanoico	PFUnDA	2058-94-8
Ácido Perfluorododecanoico	PFDoDA	307-55-1
Ácido Perfluorotridecanoico	PFTrDA	72629-94-8
Ácido Perfluorotetradecanoico	PFTeDA	376-06-7
Ácido Perfluorohexadecanoico	PFHxDA	67905-19-5
Ácido Perfluorooctadecanoico	PFODA	16517-11-6
Ácido Dímero de óxido de Hexafluoropropileno	HFPO-DA	13252-13-6

Ácido 4,8-Dioxa-3H-perfluorononanoico	DONA	919005-14-4
Ácido Perfluorobutano sulfónico	PFBS	375-73-5
Ácido Perfluoropentano sulfónico	PFPeS	2706-91-4
Ácido Perfluorohexano sulfónico	PFHxS	355-46-4
Ácido Perfluoroheptano sulfónico	PFHpS	375-92-8
Ácido Perfluorooctano sulfónico (lineal)	PFOS	1763-23-1
Ácido Perfluorooctano sulfónico (ramificado)	PFOS Br	1763-23-1
Ácido Perfluorononano sulfónico	PFNS	98789-57-2
Ácido Perfluorodecano sulfónico	PFDS	2706-91-4
Ácido 9-chlorohexadecafluoro-3-oxanonano-1-sulfónico	9ClPF3OUdS	756426-58-1
Ácido 11-chloroeicosafluoro-3-oxaundecano-1-sulfónico	11ClPF30UdS	763051-92-9
Ácido 4:2 Fluorotelomero sulfónico	4:2 FTS	757124-72-4
Ácido 6:2 Fluorotelomero sulfónico	6:2 FTS	27619-97-2
Ácido 8:2 Fluorotelomero sulfónico	8:2 FTS	39108-34-4
Ácido 10:2 Fluorotelomero sulfónico	10:2 FTS	120226-60-0
Perfluorooctano sulfonamida	PFOSA	754-91-6
N-Metilperfluorooctano sulfonamida	N-MeFOSA	31506-32-8
N-Metilperfluorooctanosulfonamido acético	N-MeFOSAA	2355-31-9
N-etilperfluorooctano sulfonamida	N-EtFOSA	4151-50-2
N-Etilperfluorooctanosulfonamido acético	N-EtFOSAA	2991-50-6
4:2 Fluorotelomero fosfato monoester	4:2 mPAP	150065-76-2
6:2 Fluorotelomero fosfato monoester	6:2 mPAP	57678-01-0
8:2 Fluorotelomero fosfato monoester	8:2 mPAP	57678-03-2
6:2 Fluorotelomero fosfato diéster	6:2/6:2 diPAP	57677-95-9
8:2 Fluorotelomero fosfato diester	8:2/8:2 diPAP	678-41-1
10:2 Fluorotelomero fosfato diester	10:2/10:2 diPAP	1895-26-7
6:2 Fluorotelomero fosfato triéster	6:2/6:2/6:2 triPAP	-

3.2. Matrices estudiadas

3.2.1. Polvo doméstico

El polvo doméstico es una matriz que está teniendo auge en su estudio como fuente de contaminación debido a que actualmente pasamos aproximadamente un 90% del tiempo en interiores. Por ello, resulta de gran relevancia su estudio, puesto que la contaminación interior ha sido relacionada con algunas enfermedades como irritación de ojos y/o piel, asma, cáncer, etc. [81]. Dicha contaminación no está regulada, y algunos estudios muestran niveles de concentración de compuestos (muchos de ellos emergentes) del orden de $\mu g \cdot g^{-1}$ hasta $mg \cdot g^{-1}$ [82,83], resultando ser un reservorio sobre todo de contaminantes semi-volátiles y no volátiles.

Aunque se trata de una matriz compleja difícil de analizar, pues contiene desde residuos biológicos como piel, cabello, ácaros, etc. hasta fibras de tejidos, residuos de combustión del tabaco o la cocina, etc. [84] que pueden ser interferentes durante el análisis, el polvo muestra un bajo nivel de variabilidad en cuanto a concentraciones de contaminantes se refiere. Es decir, debido a que no existen condiciones meteorológicas extremas como en el exterior que puedan favorecer su degradación o su dispersión, los contaminantes pueden permanecer inalterados [85]. Además, también tienen una fuerte correlación con otras matrices de interior (como aire o partículas en suspensión) y biológicas (como sangre, orina, cabello, etc.), pudiéndose hacer estudios estadísticos que relacionen la presencia de estos contaminantes con su presencia en otros microambientes y con enfermedades.

De hecho, existen fórmulas para calcular la ingestión de contaminantes, y de esta forma, poder estudiar el nivel de exposición en determinados microambientes. Se define microambiente como un espacio delimitado con unas características específicas como temperatura, humedad, cantidad de luz, etc. Así, por ejemplo, un microambiente podría ser desde la habitación de una casa o una oficina de trabajo, hasta el interior de un coche. A

continuación, se muestra un ejemplo de fórmula para el cálculo de la exposición humana diaria a contaminantes a través de la ingestión de polvo (en ng/día) [86]:

$$\sum_{(evdi)} = [(C_H F_H) + (C_O F_O) + (C_C F_C) + (C_P F_P)] \cdot RR$$

donde C es la concentración (ng $\cdot g^{-1}$) de casas (C_H), oficinas (C_o), coches (C_c) y lugares públicos (C_P); F es la fracción (%) de tiempo que estamos en cada lugar: 63.8% y 86.1% en casas (F_H), 22.3% y 0% en oficinas (F_o), 4.1% y 4.1% en coches (F_c) y 5.1% y 5.1% en lugares públicos (F_P), para adultos y niños pequeños, respectivamente [87]; y RR es el ratio de ingestión diaria (mg/día) [86] que puede ser 20 mg/día para adultos y 40 mg/día para niños pequeños en un caso normal, mientras que en un caso extremo, se considera 60 mg/día para adultos y 100 mg/día para niños pequeños [88].

3.2.2. Envases de alimentos

Otras fuentes de exposición importantes son los alimentos y sus envases, ya que estos últimos suelen contener compuestos tóxicos, que pueden migrar fácilmente al alimento contaminándolo. La normativa general europea que regula los materiales destinados a estar en contacto con alimentos (desde los equipos que los procesan, hasta utensilios de cocina y envases), conocidos como *FCMs* (de sus siglas en inglés *Food Contact Materials*) se recoge en el Reglamento General CE 1935/2004 y en el Reglamento sobre buenas prácticas de producción de FCMs (CE) 2023/2006. Debido a que cada vez hay más estudios donde se relacionan algunas enfermedades con determinados compuestos contaminantes en los productos de uso cotidiano [89,90], la seguridad química de los FCMs es una prioridad para la Autoridad Europea de Seguridad Alimentaria (*EFSA*, de sus siglas en inglés *European Food Safety Authority*) [91,92].

Sin embargo, las restricciones europeas solo son aplicadas a una parte del total de estos materiales (plásticos nuevos y reciclados, cerámicas, celulosa regenerada y materiales activos e inteligentes), habiendo otros (conocidos como FCMs no armonizados) cuyas restricciones son a nivel nacional (siendo diferentes entre distintos países) o incluso inexistentes.

Existen unas 8.000 sustancias reguladas en FMCs aproximadamente, tanto autorizadas como prohibidas o limitadas hasta un cierto nivel, en función de la exposición humana a ellas o su toxicidad. Sin embargo, no se tienen en cuenta las denominadas sustancias añadidas de forma no intencionada (*NIAS*, de sus siglas en inglés *non-intentionally added compounds*,), que son impurezas, subproductos o productos de degradación originados en el procesamiento de los alimentos o causados por el reciclaje, y que podrían constituir la mayoría de sustancias químicas presentes en un producto [93]. Tampoco se tienen en cuenta los efectos de la combinación de múltiples compuestos que conforman un FMC, ya que las actuales regulaciones consideran cada contaminante por separado a la hora de evaluar su potencial toxicidad. Por ello, resulta de gran relevancia el estudio de estos materiales para proporcionar información a las autoridades con competencias en legislación con el fin de restringir o limitar el uso de determinadas sustancias que suponen un riesgo para la salud.

3.2.3. Papel térmico

El papel térmico se trata de un material utilizado sobre todo en tickets de compra o billetes de transporte público, donde el BPA se utiliza como revelador del color [94]. El BPA reacciona con el tinte del papel térmico cuando se calienta con un láser, produciendo un complejo coloreado [95]. Al contrario que en los plásticos donde el BPA se encuentra polimerizado, en el papel térmico se encuentra en su forma libre, siendo aplicado sobre

la superficie en cantidades que alcanzan los miligramos, lo que supone un riesgo para la salud a través de la exposición dérmica. Dicha exposición depende de diversos factores tales como la concentración de BPA en el material, su transferencia a la piel, la superficie de contacto con el papel y el tiempo de duración, así como las veces que ocurre diariamente [94]. También se ha demostrado que la exposición se incrementa unas diez veces si la piel está húmeda o grasa [96].

El papel térmico es considerado la segunda fuente de exposición externa al BPA para la población mayor de 3 años. Por ello, el uso de BPA ha sido restringido en este material en 2020, donde su concentración no puede ser superior al 0.02% del peso del ticket [97]. Otras estrategias han sido la introducción de compuestos análogos al BPA, como el BPS o BPF, que aunque también presentan alteración en la actividad endocrina [96], su efecto es inferior al del BPA.

En este contexto, la evaluación de la contaminación global a la que estamos sometidos a diario es crucial. Para ello, es necesario el desarrollo de análisis de multi-componentes en una variedad de matrices con el fin de obtener la máxima información en el menor tiempo posible, con el objetivo de proporcionar herramientas tanto a la industria como a las instituciones que faciliten la toma de decisiones.

3.3. Disolventes supramoleculares

El estudio de ECs es complejo debido a la gran cantidad de compuestos estructuralmente diferentes que engloba, y a la amplia variedad de matrices en las que se encuentran. En los métodos analíticos reportados hasta la fecha para la determinación de ECs se aplican dos estrategias en función del estado de la muestra. El análisis de muestras sólidas requiere una primera etapa de extracción con disolventes orgánicos, generalmente metanol, diclorometano, hexano, etc., y posteriormente, se suele aplicar una etapa de limpieza de la muestra, generalmente con extracción en fase sólida (SPE), seguida de evaporación/reconstitución del extracto para alcanzar la sensibilidad requerida. En el caso de muestras líquidas, la técnica de extracción más utilizada es SPE. Estas estrategias requieren por lo general de un elevado consumo de disolventes orgánicos [98] y varias etapas que son lentas y tediosas, y por lo tanto poco apropiadas para la monitorización de ECs en el medioambiente y en estudios epidemiológicos dirigidos a evaluar la exposición humana a estos contaminantes.

Actualmente, uno de los campos más punteros en la química analítica es la búsqueda de procesos de extracción más simples, miniaturizados y ecológicos, entre otras características. Es decir, se busca que sigan los 12 principios de la Química Sostenible (Ver figura 1). Como la tendencia es reducir el consumo de disolventes orgánicos, se tiende al empleo de técnicas miniaturizadas como la microextracción en fase sólida (*SPME*, de sus siglas en inglés *solid-phase microextraction*) [99,100] y al incremento de la eficiencia mediante la aplicación de energías auxiliares como microondas, sonicación o el uso de líquidos presurizados [3,99,100]. Pero aún así no se evitan etapas posteriores de limpieza que además de consumir disolventes orgánicos, se incrementa el riesgo de pérdida de contaminantes.

Figura 1. *Principios de la Química Sostenible.*

En 2020, se adoptó el Pacto Verde Europeo (*European Green Deal*) con el fin de desarrollar una economía más eficiente y competitiva con respecto al uso de los recursos. Esto, junto con las regulaciones cada vez más estrictas sobre las emisiones de compuestos orgánicos volátiles y su toxicidad, ha impulsado el desarrollo de los llamados disolventes verdes, cuyo empleo está en línea con el compromiso "cero emisiones en Europa" (*Zero-Waste Europe*) [101,102]. Se define disolvente verde como aquel disolvente con un ciclo de vida sostenible que no es peligroso para la salud ni para el medio ambiente, y que se inspira en los doce principios de la Química Sostenible (Figura 1), aunque actualmente todavía no existe un disolvente que los cumpla todos [103]. Entre los disolventes desarrollados hasta la fecha, que cumplen totalmente o parcialmente con algunos de los principios de la Química Sostenible podemos citar los líquidos iónios (ionic liquids, IL), los disolventes eutécticos (deep eutectic solvents, DES), los fluídos supercríticos (supercritical fluids, SCF) y los disolventes supramoleculares (SUPRASs).

En las investigaciones presentadas en esta Tesis se han desarrollado métodos de microextracción genéricos, simples, rápidos y económicos empleando distintos SUPRASs, cuyas características y propiedades los hace idóneos para sustituir a los disolventes convencionales, pues cumplen muchos de los principios de la Química Sostenible.

Los SUPRASs son líquidos nanoestructurados producidos mediante el autoensamblaje y la coacervación de moléculas anfifílicas en medios acuosos o hidro-orgánicos [104–106]. El término SUPRAS fue acuñado por primera vez por nuestro grupo de investigación (*Supramolecular Analytical Chemistry*, SAC), con el fin de resaltar que se tratan de disolventes constituidos por la unión espontánea de moléculas mediante un fenómeno de autoensamblaje basado en interacciones no covalentes [107].

3.3.1. Formación de los SUPRASs

3.3.1.1. Autoensamblaje

El autoensamblaje se define como la asociación de anfifilos, de manera espontánea y reversible, para formar estructuras ordenadas tridimensionales cuando se encuentran por encima de su concentración de agregación crítica (*cac,* de sus siglas en inglés *critical aggregation concentration*). Al alcanzar la *cac*, las interacciones entre las moléculas anfifílicas son más favorables energéticamente que la interacciones anfifilo-disolvente, lo que conduce a su agregación. La morfología de los agregados formados depende de la estructura de las moléculas anfifílicas, así como de la composición del sistema coloidal en el que se encuentran. Las estructuras formadas son generalmente micelas acuosas o inversas,

vesículas, etc. [104], y pueden predecirse a través de la ecuación propuesta por Israelachvili [108]:

$$g = \frac{V}{a_0 l_c}$$

donde g es el factor de empaquetamiento, V es el volumen que ocupa la cadena hidrocarbonada de la molécula anfifílica y l_c es su longitud, mientras que a_0 es el área que ocupa la cabeza polar en el agregado formado.

En la Figura 2 se representan esquemáticamente distintas morfologías formadas por los agregados.

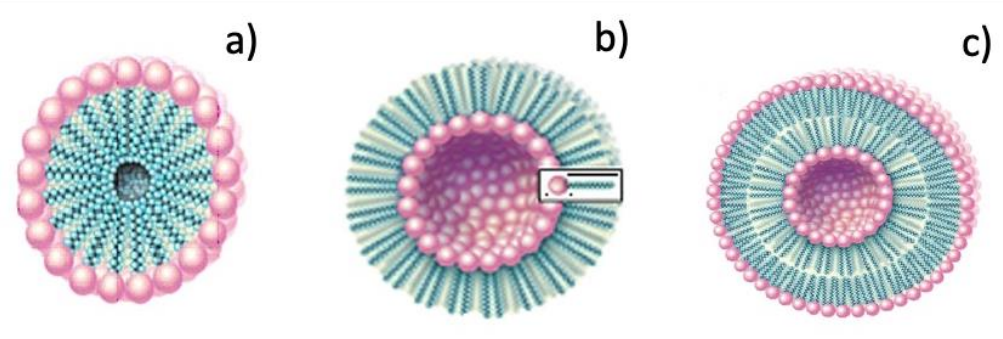


Figura 2. *Algunas de las morfologías que pueden formar las moléculas anfifílicas durante el proceso de autoensamblaje: a) micela acuosa, b) micela inversa y c) vesícula.*

3.3.1.2. Coacervación

Se denomina coacervación al proceso que tiene lugar cuando un sistema coloidal se separa en dos fases líquidas [109]. La fase con elevada concentración de anfifilo se denomina SUPRAS y se encuentra en equilibrio con la otra fase que contiene moléculas de anfifilo a la *cac*. Para que esta separación ocurra en el sistema coloidal, deben establecerse condiciones experimentales que disminuyan las fuerzas de repulsión entre las cabezas polares de los agregados coloidales, de manera que se favorezca el crecimiento de los mismos. En el proceso de coacervación, inicialmente se forman gotas de coacervado que se asocian en clústeres, los cuales tienen una densidad diferente a la disolución que las contiene, y finalmente se separan formando una nueva fase (SUPRAS), en la que los anfifilos se organizan en forma de bicapas, estructuras hexagonales inversas, estructuras esponjosas, etc. [110]. En la Figura 3 se muestra un ejemplo de la nanoestructura de un SUPRAS.

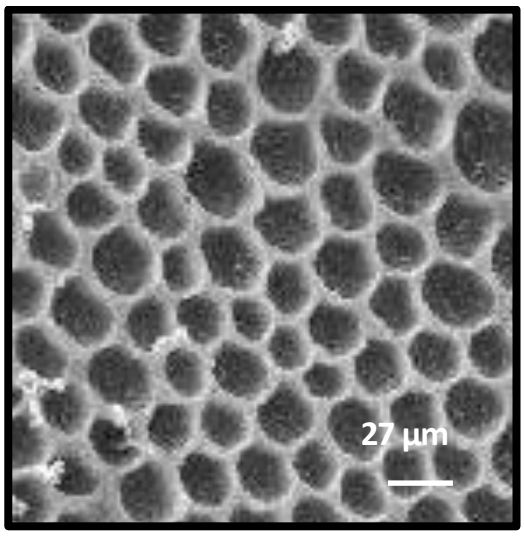


Figura 3. *Estructura hexagonal inversa de un SUPRAS formado por alcohol, tetrahidrofurano (THF) y agua como agente coacervante.*

Para provocar el cambio en las condiciones ambientales y desencadenar la coacervación, se utiliza lo que se denomina agente coacervante. En el caso de anfifilos con grupos funcionales iónicos, este agente coacervante puede ser un modificador de pH [111] o una sal orgánica o inorgánica [112]. De esta forma se neutralizan los grupos polares iónicos lo que permite mayor empaquetamiento de las moléculas anfifílicas y el crecimiento de los agregados presentes en el sistema coloidal.

Por otro lado, en el caso de anfifilos con grupos funcionales no iónicos, puede utilizarse un cambio en la temperatura para favorecer la unión entre agregados al eliminar las moléculas que solvatan los grupos polares [113], o la adición de un disolvente miscible con la disolución inicial, pero en el cual la molécula anfifílica no es soluble. De esta forma, se favorece la desolvatación de los grupos polares, y por ende, las interacciones anfifilo – anfifilo [114,115]. En la Figura 4 se muestra el proceso de formación de un SUPRAS de forma esquemática.

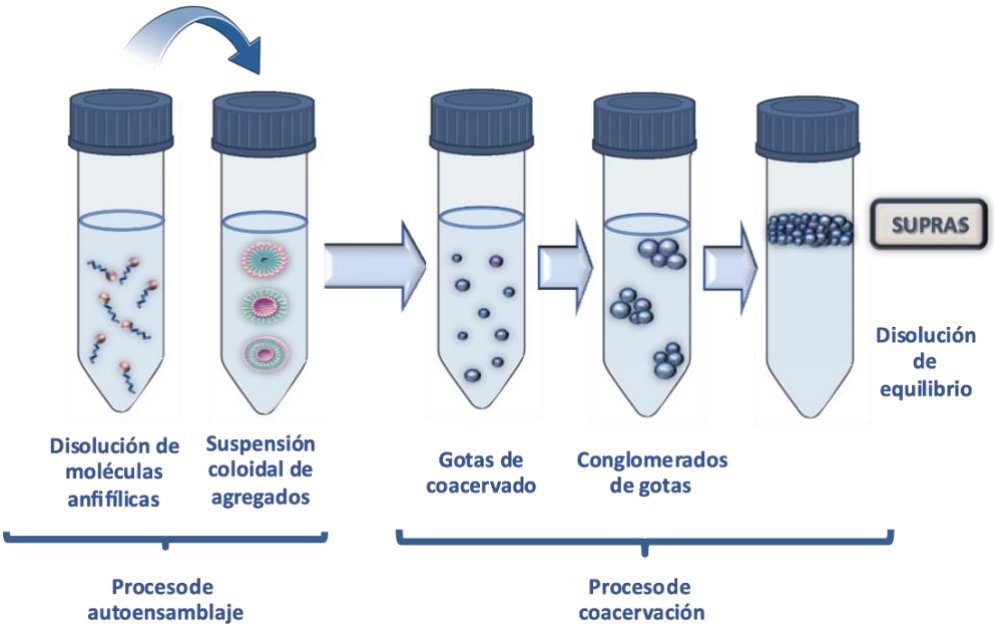


Figura 4. *Representación esquemática del proceso de formación del disolvente supramolecular (SUPRAS).*

3.3.2. Diagramas de fases

Los componentes utilizados en la formación de los SUPRAS son normalmente el anfifilo, el disolvente (que puede ser agua o disolvente orgánico dependiendo de la solubilidad del anfifilo) y el agente coacervante (sal, ácido o base, temperatura, o disolvente en el que el anfifilo no es soluble). Los diagramas de fases delimitan las condiciones experimentales en las que se forman los SUPRASs, y se construyen variando la concentración/magnitud de cada uno de los componentes que los constituyen. Visualmente, en la región de formación del SUPRAS coexistirán dos fases líquidas, siendo una el SUPRAS y la otra la fase de equilibrio. Fuera de esta región, pueden existir una gran variedad de fases dependiendo de la estructura de la molécula anfifílica y su concentración así como de la concentración/magnitud del agente coacervante. En general, en la mayoría de los diagramas de fases obtenidos existe una región correspondiente a una disolución isotrópica del anfifilo. En la Figura 5 pueden verse varios diagramas de fase correspondientes a SUPRASs de distinta composición formados con diferentes agentes coacervantes.

Las Figuras 5a y 5b son ejemplos de diagramas de fase de SUPRASs formados por anfifilos no iónicos, siendo el agente coacervante un incremento de la temperatura o la adición de agua, que es un disolvente en el que las moléculas anfifílicas no son solubles. Por otro lado, las Figuras 5c y 5d son ejemplos de diagramas de fase de SUPRASs formados con anfifilos iónicos, siendo el agente coacervante una sal para neutralizar la carga de la cabeza polar iónica de la molécula anfifílica, o la adición de ácido para la protonación del grupo funcional del anfifilo.

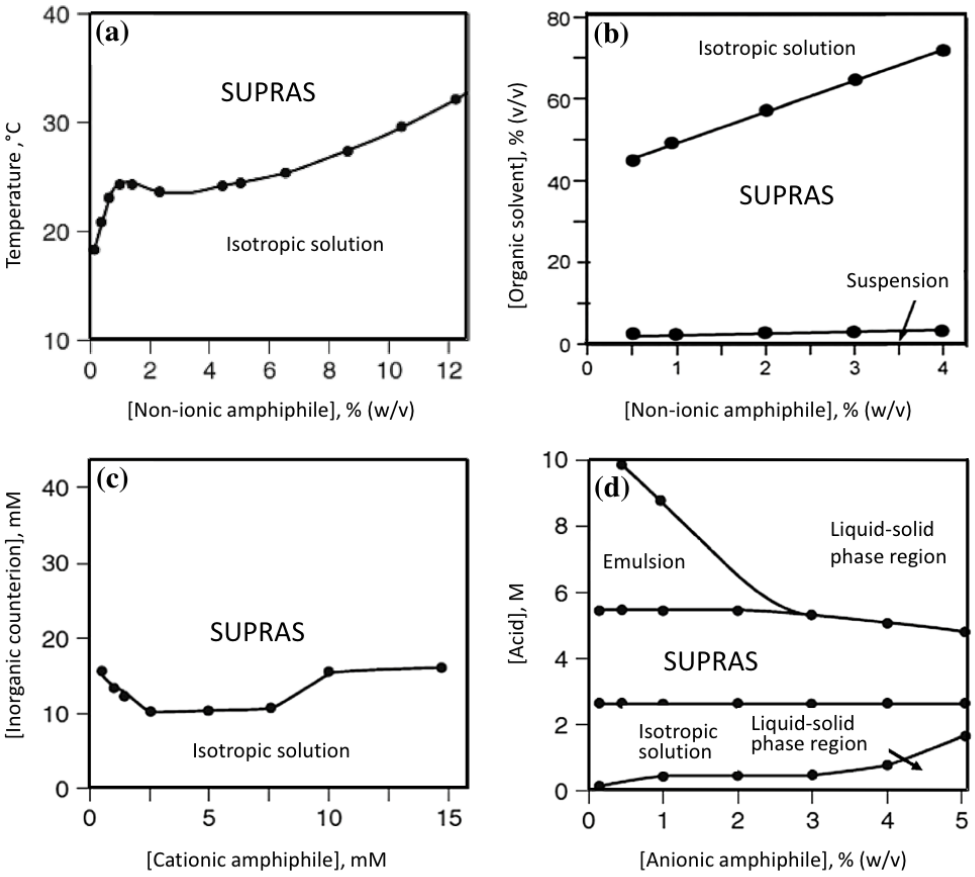


Figura 5. *Diagramas de fase de SUPRASs preparados con anfifilos no iónicos con cambio de temperatura (a) o adición de disolvente orgánico (b), y con anfifilos iónicos con adición de un contra-ion (c) o de un ácido (d). Gráficas obtenidas de los artículos:* [104,115].

El volumen de SUPRAS formado en la región de coacervación es, en la mayoría de los casos, una función lineal de la concentración de anfifilo en la disolución coloidal. Sin embargo, existen algunas excepciones como por ejemplo los SUPRASs sintetizados con Triton X-100 o PEG/PPG 18-18 dimeticona (óxido de silicona-etileno/copolímero de óxido de propileno), donde la concentración de anfifilo en el SUPRAS aumenta al incrementarse la concentración del mismo en la disolución coloidal. Por otro lado, el volumen de SUPRAS formado con agua como coacervante también es proporcional al porcentaje de disolvente orgánico en la

disolución de síntesis (v/v), puesto que este hace que el tamaño de las gotas de coacervado sea mayor [104,114]. Para este tipo de SUPRASs, sintetizados con alcoholes y ácidos carboxílicos en mezclas de THF/agua, se han obtenido ecuaciones experimentalmente que nos permiten calcular el volumen producido de SUPRASs a partir de una cantidad dada de anfifilo y de disolvente orgánico. Este aspecto es importante, ya que se puede predecir con antelación el factor de preconcentración teórico que se puede alcanzar.

En la Tabla 5 se muestran algunas de las ecuaciones calculadas experimentalmente para obtener el volumen de SUPRAS formado.

Tabla 5. Ecuaciones para calcular el volumen de SUPRAS formado a partir de alcoholes y ácidos carboxílicos como moléculas anfifílicas en mezclas de agua y THF.

Anfifilos	Nº de carbonos	Ecuación
Alcoholes	7 - 14	$V_{SUPRAS} = X(0.17 + e^{0.0389*THF})$
Ácidos carboxílicos	6	$V_{SUPRAS} = 0.60X + 0.076X * THF + e^{0.0.104*THF})$
	8	$V_{SUPRAS} = 1.17Xe^{0.039*THF}$
	10	$V_{SUPRAS} = 1.05Xe^{0.047*THF}$
	12	$V_{SUPRAS} = 0.92Xe^{0.056*THF}$

V_{SUPRAS}= volumen de SUPRAS formado (µl); X= cantidad de anfifilo en la disolución de síntesis (mg); THF= porcentaje (v/v) de THF en la disolución de síntesis.

3.3.3. Propiedades de los SUPRASs

Los SUPRASs poseen diversas propiedades intrínsecas que les confieren un gran potencial como agentes extractantes. Así, son disolventes cuyas propiedades y funcionalidades pueden modelarse mediante la selección de la estructura de la molécula anfifílica o las condiciones de coacervación (tipo y concentración de sal, pH, temperatura, etc.). Un ejemplo es el diseño de SUPRASs con propiedades de acceso restringido que tienen la capacidad de excluir macromoléculas durante el proceso de extracción de los solutos mediante mecanismos físicos y químicos [114,116].

Por otro lado, debido a la elevada concentración de anfifilo en el SUPRAS (en torno a ~ 0.1 - 1 mg·μL^{-1}), poseen un gran número de sitios de unión, por lo que pueden obtenerse factores de preconcentración bastante elevados (entre 100 - 500) debido a que pueden extraer una gran cantidad de analitos utilizando un volumen muy bajo de disolvente. Además, debido a que las gotas de coacervado permanecen como entidades individuales, el SUPRAS tiene elevada área superficial, lo que favorece que las extracciones de los compuestos sean muy rápidas.

Dichos compuestos pueden ser de diversa polaridad, ya que las moléculas anfifílicas que forman los SUPRASs poseen carácter polar debido al grupo funcional, y apolar debido a la cadena hidrocarbonada. Por lo tanto, ofrecen microambientes de diferente polaridad. La solubilización de los solutos es debida principalmente a interacciones de dispersión en la región apolar (que pueden predecirse a través de la constante octanol-agua correspondiente), mientras que en la región polar viene determinada por interacciones iónicas, puentes de hidrógeno, π-catión, etc. [104,117]. La Figura 6 muestra un ejemplo de los diferentes microambientes en un SUPRAS formado con un alcohol como molécula anfifílica, disolvente orgánico y agua. En este caso, el autoensamblaje ha dado lugar a micelas inversas (que han coacervado formando un SUPRAS con estructura hexagonal inversa) donde las cadenas hidrocarbonadas se encuentran

disueltas en el disolvente orgánico, mientras que las cabezas polares se encuentran orientadas hacia un "pool" acuoso [114].

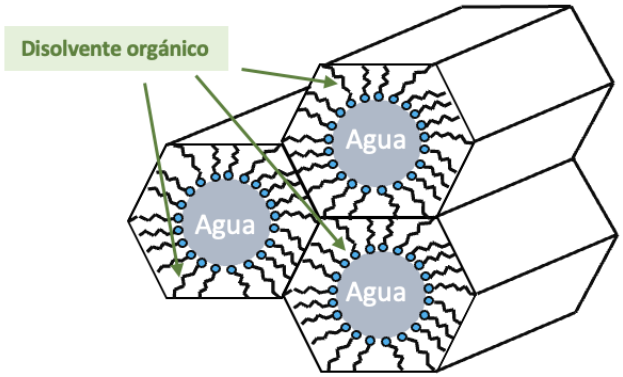


Figura 6. *Agregado hexagonal de micelas inversas de alcoholes formados en mezclas de disolvente orgánico y agua.*

Por último, otras propiedades complementarias y que también los hace ventajosos en procesos de extracción son su facilidad de preparación, ya que se trata de un proceso de síntesis que se lleva a cabo de forma espontánea y a temperatura ambiente. El proceso es atómicamente eficiente ya que prácticamente todo el anfifilo pasa a formar parte del SUPRAS. Además, la mayoría de los SUPRASs son menos volátiles e inflamables que los convencionales, por lo que permiten el desarrollo de procesos más seguros, tanto para el personal como para el medio ambiente [104,105,114,118].

Sin embargo, muchos de los SUPRASs están constituidos por moléculas anfifílicas que provienen de fuentes no renovables y que son parcialmente degradables como por ejemplo, sales de alquil amonio, sales de

alquilsulfatos y alquilsulfonatos, etc. [106]. Además, algunos SUPRASs requieren de disolventes orgánicos como metanol o THF, e incluso en ocasiones, necesitan de condiciones muy ácidas o elevadas temperaturas para coacervar [111,119]. Esto compromete la sostenibilidad de los SUPRASs, por lo que recientemente nuestro grupo se ha enfocado en el desarrollo de SUPRASs sintetizados a partir de ácidos grasos y alcoholes en mezclas de etanol y agua [120,121], denominándolos BioSUPRASs. El *capítulo IV* de esta Tesis se enfoca en el desarrollo de uno de estos SUPRASs sostenible mediante el uso de metil-tetrahidrofurano, que es un disolvente orgánico verde que sustituye al THF, pero cumple con las mismas funciones al tener una estructura similar [122].

Todas estas propiedades hacen de los SUPRASs excelentes candidatos para el tratamiento genérico de muestras, como el polvo o los alimentos, que son matrices heterogéneas y complejas [107,123–127]. Los SUPRASs son disolventes a medida, como se ha mencionado anteriormente, cuya composición y nanoestructura puede cambiar según la naturaleza de la disolución de síntesis [114,116]. Ambos aspectos influyen en la extracción de los compuestos de interés y la simultánea exclusión de las interferencias (gracias a sus propiedades de acceso restringido). Por ejemplo, los SUPRASs formados con disolvente orgánico, agua como agente coacervante y alcoholes o ácidos carboxílicos como anfifilos, tienen menos contenido en agua cuando las cadenas hidrocarbonadas de las moléculas anfifílicas son más largas, es decir, son SUPRASs con menos sitios de unión para la extracción de compuestos polares, favoreciéndose la extracción de los apolares [104]. Por otro lado, los SUPRASs con mayor contenido en agua en la disolución de síntesis inicial dan lugar a gotas de coacervado más grandes y estructuras menos empaquetadas, con mayor cantidad de agua, lo que resulta en mejores eficiencias de extracción para compuestos polares y moderadamente polares, como por ejemplo, los bisfenoles [128,129].

3.3.4. Formatos de extracción con SUPRASs

Los formatos de extracción con SUPRASs que existen son *in situ* y *ex situ*, y el empleo de uno u otro depende de la naturaleza de la muestra. Así, la extracción *in situ* puede ser usada para muestras líquidas o sólidas, mientras que la extracción *ex situ* se ha utilizado hasta la fecha preferencialmente para muestras sólidas.

3.3.4.1. Extracción con SUPRASs *in situ*

La extracción *in situ* implica la formación del SUPRAS en presencia de la muestra (líquida o sólida), produciéndose la extracción de los compuestos de interés al mismo tiempo. Para ello se realiza un proceso de agitación, con el fin de favorecer el contacto entre los componentes que forman el SUPRASs, y a la vez, de éste con los analitos a extraer, y otro proceso posterior de centrifugación, para acelerar la separación de fases. En el caso de muestras líquidas se formarán dos fases: una correspondiente al SUPRAS (que puede estar en la parte superior o inferior, según la densidad y que dependerá del anfifilo utilizado [106,115,117]) y que contendrá los analitos de interés, y otra que será la fase de equilibrio. En el caso de muestras sólidas, se formarán tres fases: las dos fases descritas anteriormente, y una tercera fase sólida que se corresponde con la muestra.

Para separar las fases, si el SUPRAS tiene una densidad inferior que la fase de equilibrio, y por tanto, se queda flotando sobre ésta, la recuperación es más sencilla, ya que puede cogerse con una micropipeta directamente y transferirse a un vial para su posterior medición. Si por el contrario el SUPRAS tiene una densidad mayor a la de la fase de equilibrio, quedando ésta en la zona superior, se puede enfriar el tubo tras la centrifugación con el fin de aumentar la viscosidad del SUPRAS, que se adherirá a las paredes facilitando así el desecho de la fase de equilibrio por decantación. Algunos

ejemplos de la extracción *in situ* con SUPRAS son por ejemplo la determinación de drogas de abuso en agua de grifo [130], contaminantes en agua naturales [131], antioxidantes en aguas residuales de tratamiento del café [132], drogas [133] o medicamentos [134] en orina, o bisfenoles en distintos alimentos líquidos [135]. En estas aplicaciones, la propia muestra aporta el agua necesaria para la formación del SUPRAS, bien porque es una muestra acuosa o bien porque tiene un alto contenido acuoso.

3.3.4.2. Extracción con SUPRASs *ex situ*

En la extracción *ex situ*, el SUPRAS es formado en una primera etapa (como se describe en la sección 3.3.1.), y posteriormente añadido a la muestra, generalmente sólida. En el caso de que los compuestos de interés sean apolares, la adición de la fase de equilibrio es recomendable, ya que esta actúa como "sumidero" para los compuestos más polares, por lo que ayuda en la eliminación de interferencias. Por el contrario, si los compuestos a extraer son polares, la fase de equilibrio debe añadirse en una menor proporción para no perder eficiencia de extracción. Es aconsejable añadir siempre un poco de fase de equilibrio para humectar la muestra, sobre todo cuando son muestras muy secas o están liofilizadas.

3.3.5. Compatibilidad del SUPRAS con las técnicas analíticas de medida

Otra propiedad de los SUPRASs es su compatibilidad con las técnicas analíticas utilizadas para determinar los compuestos de interés, como por ejemplo, la cromatografía líquida (LC) acoplada a detectores de fluorescencia, UV-visible o espectrometría de masas (MS, de sus siglas en inglés *Mass Spectrometry*).

Tras la extracción, los extractos de SUPRASs conteniendo los analitos pueden ser inyectados directamente en LC, sin necesidad de clean-up o dilución. Al entrar en contacto el SUPRAS con la fase móvil, los agregados se destruyen al cambiar las condiciones ambientales, produciendo una elevada concentración de monómeros de moléculas anfifílicas que en la columna se separan de los analitos, no interfiriendo en su separación o medida. Además, pueden desecharse antes de llegar al detector, generando así cromatogramas más limpios, y en el caso de detectores como el espectrómetro de masas (MS), se evita que la fuente se ensucie en exceso o que la ionización de algún compuesto se vea comprometida. Por otro lado, cuando se usan fases móviles con un alto contenido en agua (por encima del 40%), los agregados del SUPRAS se destruyen más lentamente a lo largo del sistema cromatográfico, dando lugar a "pseudofases" donde los analitos pueden distribuirse, afectando a su resolución. Para evitar esto, se recomienda diluir el extracto con un disolvente orgánico [106,117].

En el caso de la cromatografía de gases (GC), no se han obtenido buenos resultados hasta la fecha en cuanto a su introducción directa en el equipo. Algunas de las estrategias seguidas son la eliminación de las moléculas anfifílicas mediante extracción en fase sólida o su derivatización, o la re-extracción líquido-líquido de los analitos en otro disolvente, previo a su introducción en el sistema [106,117].

Los SUPRASs se han empleado con éxito en la extracción de una gran variedad de contaminantes orgánicos en muestras medioambientales,

biológicas y de alimentos [106]. En la siguiente tabla (Tabla 6) se muestran algunas de sus aplicaciones en los últimos 5 años.

Tabla 6. Aplicaciones de los SUPRAS para la extracción de distintos compuestos en diferentes matrices, así como los componentes necesarios para su formación y la técnica analítica utilizada para medir.

Compuestos	Matriz	a. Tensioactivo b. Disolvente	Agente coacervante	Técnica analítica	Ref.
Drogas de abuso	Agua de grifo	a. 1-Hexanol b. THF	La propia muestra (agua)	LC-MS/MS	[130]
Opioides, cocaína y anfetaminas	Pelo humano	a. 1-Hexanol b. THF	Agua	LC-MS/MS	[136]
Polifenoles	Biomasa vegetal (frambuesas)	a. 1,2-octanodiol o 1-octanol b. THF, 1-propanol o etanol	Agua	LC-MS/MS	[137]
Hidrocarburos policíclicos aromáticos (PAHs)	Suelos	a. Ácidos carboxílicos b. THF	Agua	LC-FL	[138]
Bisfenoles	Polvo doméstico de invernadero	a. 1-Hexanol b. THF	Agua	LC-MS/MS	[123]
Drogas de dopaje	Orina	a. 1,2-hexanodiol b. Agua de la propia muestra	Sal	LC-MS/MS	[133]
Colorantes	Agua	a. Ramnolípidos b. La propia muestra (agua)	Disolución de ácido clorhídrico	LC-MS/MS	[131]
Benzodiacepinas	Orina	a. 1-Hexanol b. THF	Agua de la propia muestra	LC-MS/MS	[134]
Bisfenoles	Latas de refrescos y comida, botellas de agua, polvo doméstico, orina y suero.	a. 1-Hexanol b. THF	Agua de la propia muestra	LC-MS/MS	[135]

Opiorfina	Saliva	a. Ácido Heptafluorobutírico b. Agua de la propia muestra	Disolución de ácido clorhídrico	LC-MS/MS	[139]
Compuestos antioxidantes	Pulpa de café	a. Ácido octanoico b. Etanol	Agua	LC-MS/MS	[140]
Cafeína y compuestos antioxidantes	Aguas residuales de la producción de café	a. 1-hexanol o ácido decanoico b. Etanol	La propia muestra (agua)	LC-UV	[132]
Fitohormonas	Tejido vegetal	a. 1-Hexanol b. THF	Agua	LC-MS/MS	[141]
Carotenoides y polifenoles	Biomasa vegetal (microalgas)	a. Ácido octanoico b. Etanol	Agua acidificada	LC-MS/MS	[121]
Permetrina	Frutas y vegetales	a. 1-Hexanol b. THF	Agua	LC-MS/MS	[142]
Cocidiostatos	Alimentos	a. 1-Hexanol b. THF	Agua	LC-MS/MS	[143]
Principios activos farmacéuticos y excipientes	Medicamentos	a. Ácido poliundecilénico b. Tetraglima.	Agua	GC-MS	[144]
Benzimidazol	Leche	a. 1-Hexanol b. THF	Agua de la propia muestra	LC-MS/MS	[145]
Astaxantina	Microalgas	a. Ácido octanoico b. Etanol	Disolución de ácido clorhídrico	LC-UV	[146]
Colorantes	Agua	a. Ácido decanoico o decanoato b. Iones tetraalquil amonio (butil, pentil o hexil)	La propia muestra (agua)	LC-FL	[147]

Enantiómero de hexabromociclododecano	Agua	a. Ácido decanoico b. THF	La propia muestra (agua)	LC-MS/MS	[148]
Bisfenoles	Saliva	a. 1-Hexanol b. THF	Agua de la propia muestra	LC-MS/MS	[149]
PAHs hidroxilados	Orina	a. Ácido decanoico b. THF	Agua de la propia muestra	LC-MS/MS	[150]
Anfetaminas	Saliva, orina, suero, sudor, leche materna	a. 1-Hexanol b. THF	Agua de la propia muestra	LC-MS/MS	[151]
Ocratoxina A	Especias	a. Ácido decanoico b. THF	Disolución de ácido clorhídrico	LC-FL	[152]
Enantiómeros hexabromociclododecano	Suelos y sedimentos	a. Ácido decanoico b. THF	Agua	LC-MS/MS	[153]
Micotoxinas	Cereales	a. Ácido oleico b. THF	Disolución de ácido clorhídrico	LC-MS/MS	[154]
Micotoxinas	Alimentos (vino, especias, cereales trigo)	a. Ácido tetradecanoico b. THF	Agua	ELISA	[155]
Ibuprofeno, naproxeno y ketoprofeno	Peces	a. Ácido decanoico b. THF	Agua	LC-MS/MS	[156]
PAHs	Musgo	a. Ácido decanoico b. THF	Disolución de ácido clorhídrico	LC-FL	[157]

3.4. Espectrometría de masas ambiental (AMS)

La espectrometría de masas ambiental (*AMS*, de sus siglas en inglés *Ambient Mass Spectrometry*) es una modalidad de MS, que consiste en introducir directamente la muestra (sólida o líquida) en una fuente de ionización modificada. Es decir, no se necesita de ninguna técnica de separación previa, como LC o GC, tradicionalmente acopladas a MS para separar los analitos antes de su medida. AMS ha sido usada en varios campos como el alimentario [158], medioambiental [159] o forense [160].

Se trata de una técnica relativamente reciente y muy diversificada. La primera variante fue publicada en 2004 por Takáts et al., y se denominó DESI (de sus siglas en inglés *Desorption Electrospray Ionization*). Consiste en el uso de un líquido nebulizado mediante electro-espray que impacta sobre la muestra, desorbiendo los iones de la matriz que entran directamente al MS [161]. Un poco más tarde, en 2005, Cody et al. publicaron la técnica DART (de sus siglas en inglés *Direct Analysis in Real Time*), que se basa en el uso de especies en un estado electrónico o vibracional excitado, que reaccionan con las moléculas de la muestra para producir los iones que entran directamente al MS [162]. Otra variante fue publicada por McEwen et al. en 2005, que se denominó ASAP (de sus siglas en inglés *Atmospheric Solid Analysis Probe).* Esta consiste en la utilización de un capilar de vidrio, denominado sonda, donde la muestra es cargada e introducida en una fuente de ionización a presión atmosférica (APCI, de sus siglas en inglés *Atomspheric Pressure Chemical Ionization*) modificada. Una corriente caliente de gas nitrógeno provoca la desorción de los analitos de la matriz, y su vez, debido a su cercanía a la aguja de descarga (o corona de descarga), estos analitos son ionizados [163,164], formándose radicales $M^{+\cdot}$ o iones del tipo $[M+H]^+$ o $[M-H]^-$ según la polaridad (positiva o negativa respectivamente). Los compuestos deben ser volátiles o semivolátiles (con temperaturas de evaporación por debajo de los 500ºC, al igual que en DART y DESI). Una de las principales ventajas de la técnica ASAP es que la totalidad de la muestra es introducida en la cámara de la fuente de ionización, y no solo el vapor

ionizado producido, como ocurre en las técnicas mencionadas anteriormente, lo que hace que mejore enormemente la sensibilidad [165,166]. Es por ello que esta técnica ha sido seleccionada para las investigaciones realizadas en la presente Tesis. En la Figura 7 pueden verse las distintas partes de una fuente APCI modificada para su uso en la técnica ASAP.

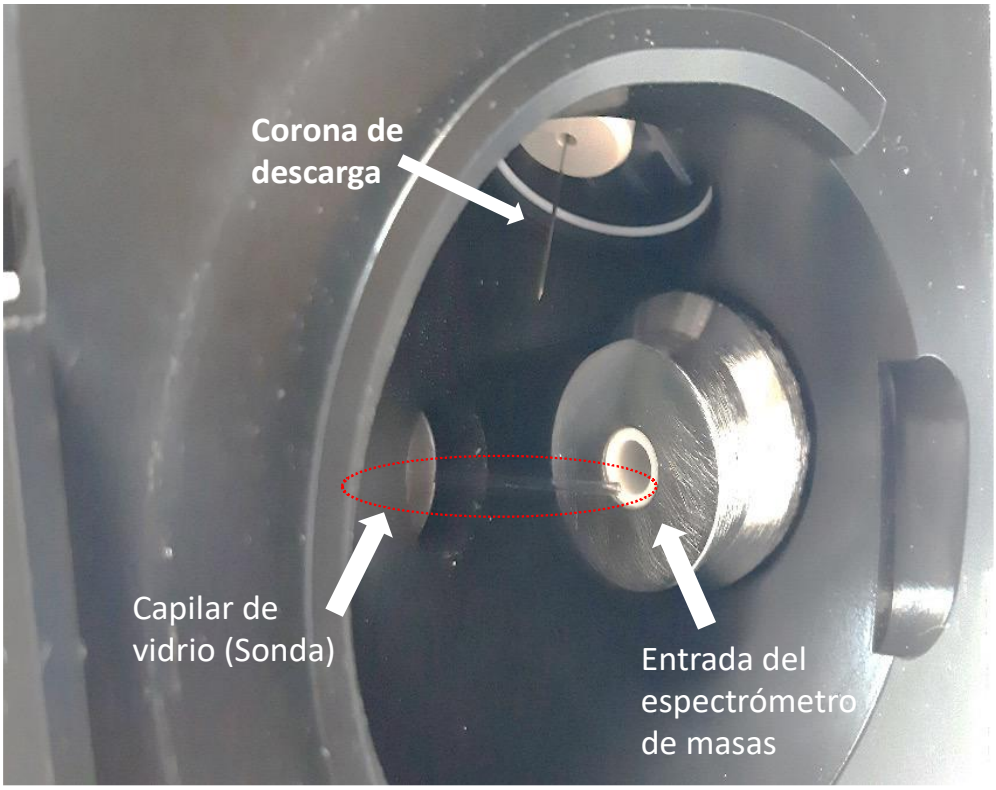


Figura 7. *Fuente de APCI modificada para su uso en la técnica ASAP. Indicadas con flechas están la corona de descarga (o aguja de descarga), la entrada del espectrómetro de masas y la sonda que contiene a la muestra.*

En la siguiente tabla (Tabla 7) se muestran todas las variantes de AMS que existen actualmente, así como la referencia en la que se describieron por primera vez. Esta gran variedad ha surgido a través de la necesidad de aplicar las primeras modalidades desarrolladas de AMS a otros tipos de muestra, consistiendo algunas de ellas en acoplamientos de dos o más modalidades en una sola fuente [167].

Tabla 7. Abreviatura, nombre en inglés de las distintas modalidades de AMS y referencia de la primera vez que fue publicada.

Abreviatura	Nombre	Referencia
DESI	Desorption Electrospray Ionization	[161]
EASI	Easy Ambient Sonic Spray Ionization	[168]
DAPPI	Desorption Atmospheric-Pressure Photoionization	[169]
DICE	Desorption Ionization by Charge Exchange	[170]
LMJ-SSP	Liquid Microjunction-Surface Sampling Probe (flowprobe)	[171]
LESA	Liquid-Extraction Surface Analysis	[172]
DART	Direct Analysis in Real Time	[162]
FAPA	Flowing Atmospheric-Pressure Afterglow	[173]
ASAP	Atmospheric Solid Analysis Probe	[164]
LTP	Low-Temperature Plasma Probe	[174]
DAPCI	Desorption Atmospheric-pressure Chemical Ionization	[175]
DBDI	Dielectric Barrier Discharge Ionization	[176]
DCBI	Desorption Corona Beam Ionization	[177]
PADI	Plasma-Assited Desorption Ionization	[178]
APTDI	Atmospheric-Pressure Thermal Desorption/Ionization	[179]
HAPGDI	Helium Atmospheric-Pressure Glow-Discharge Ionization	[180]
PPAMS LTP	Plasma Pencil Atmospheric Mass Spectrometry LTP	[181]
Ambient MHCD	Ambient Microhollow Cathode Discharge Ionization	[182]
ND-EESI	Neutral Desorption Extractive Electrospray Ionization	[183]

BADCI	Beta Electron-Assited Direct Chemical Ionization	[184]
AP-TD/SI	Atmospheric-Pressure Thermal Desorption-Secondary Ionization	[185]
PESI	Probe Electrospray Ionization	[186]
ELDI	Electrospray-Assisted Laser Desorption Ionization	[187]
MALDESI	Matrix-Assited Laser Desorption Electrospray Ionization	[188]
LAEIS	Laser-Ablation Electrospray Ionization Mass Spectrometry	[189]
LADESI	Laser-Assited Desorption Electrospray Ionization	[190]
LDESI	Laser-Desorption Electrospray Ionization	[191]
LEMS	Laser Electrospray Mass Spectrometry	[192]
LD-APCI	Laser-Desorption Atmospheric-Pressure Chemical Ionization	[193]
IR-LAMICI	Infrared Laser-Ablation Metastable-Induced Chemical Ionization	[194]
PAMLDI	Plasma-Assited Multiwavelength Laser Desorption Ionization	[195]
LAAPPI	Laser-Ablation Atmospheric-Pressure Photoionization	[196]
RADIO	Radio-Frequency Acoustic Desorption and Ionization	[197]
LIAD/ESI	Laser-Induced Acoustic Desorption-Electrospray Ionization	[198]
LIAD/APCI	Laser-Induced Acoustic Desorption-Atmospheric-Pressure Chemical Ionization	[199]
SAWN	Surface Acoustic Wave Nebulization	[200]

DEMI	Desorption Electrospray/Metastable-Induced Ionization	[201]
REIMS	Rapid Evaporative Ionization Mass Spectrometry	[202]
LDI	Laser-Desorption Ionization	[203]
SWIFERR	Swithed Ferroelectric Plasma Ionizer	[204]
LSI	Laserspray Ionization	[205]

Adaptación de la tabla publicada por Monge et al. (2014) [206].

Algunas de las ventajas del uso de AMS son su simplicidad y ahorro de costes. Así, se requiere mínimo volumen de disolvente y el análisis de la muestra se realiza de forma directa sin necesidad de un tratamiento laborioso. Es decir, la técnica permite la preparación de la muestra durante el análisis, como por ejemplo extracción líquido-sólido en el caso de DESI o desorción térmica en la técnica DART, no siendo necesarios etapas adicionales en la mayoría de las ocasiones (clean-up, preconcentración, etc). Además, la cantidad de muestra necesaria para el análisis es muy pequeña, lo que es esencial en el análisis de muestras biológicas, arqueológicas, de arte, etc.

El desarrollo de instrumentos MS portables y su acoplamiento con estas fuentes de ionización ambiental ha supuesto una revolución con respecto al análisis de muestra, pudiéndose hacer la medida *in situ*, Esto supone una ventaja con respecto al procedimiento habitual en el que se requiere la preservación de la muestra tras su recolección y el transporte y almacenaje de la misma [207]. En cuanto a la automatización, se han conseguido desarrollar algunos métodos de determinación automatizados donde el operador no tiene que estar completamente pendiente del análisis (ya que la introducción de la muestra es manual e individual), como por ejemplo un estudio donde se determinaron productos farmacéuticos utilizando una cinta en movimiento unida a una fuente DART [208], o el desarrollo AMS imaging (AMSI), publicado por primera vez por el grupo de Cooks en 2007, que consistía en el acoplamiento de la técnica DESI con

una plataforma de superficie móvil automatizada para obtener imágenes químicas 2D mediante un barrido sobre la superficie de la muestra [209].

Por otro lado, AMS también se ha utilizado para métodos de cribado con buenos resultados. De esta forma se ahorra tiempo y consumo de disolventes orgánicos [210,211]. Sin embargo, todavía existen algunos inconvenientes con respecto a su uso en este tipo de análisis, ya que la ausencia de extracción, clean-up y separación mediante cromatografía genera en muchas ocasiones espectros complejos difíciles de interpretar, supresión de la señal y baja selectividad y sensibilidad. El uso de procesos adicionales de extracción y clean-up podrían extender el uso de AMS a muestras más complejas, a la vez que mejorar la sensibilidad y la reproducibilidad. Por ello, se han desarrollado estrategias como las puntas de electrospray modificadas [212], la microextración de tipo *slug-flow* [213] o SPME [214]. Sin embargo, también tienen limitaciones en la extracción de algunos grupos de contaminantes, por lo que dificulta su uso en métodos de cribado.

En este contexto, los SUPRAS cumplen con los requisitos para trabajar con la técnica ASAP. Además de las propiedades extractantes mencionadas previamente, la elevada tensión superficial de los SUPRAS y su baja volatilidad permite su fácil introducción dentro de los capilares de vidrio. Este potencial de los SUPRAS, es el que nos ha llevado a desarrollar las investigaciones que se presentan en los capítulos *VI y VII* de esta Tesis, en los que se estudia el uso de los SUPRASs para la extracción de contaminantes previo a su análisis con la técnica ASAP. También se ha investigado la posibilidad de usar los SUPRAS-ASAP para cuantificación de contaminantes, un aspecto de gran interés para extender el uso de AMS [215,216].

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4.

Results

Block I:

Development of analytical strategies for the determination of emerging contaminants.

Chemosphere
222 (2019) 22-28

Supramolecular solvent-based microextraction of emerging bisphenol A replacements (colour developers) in indoor dust from public Environments

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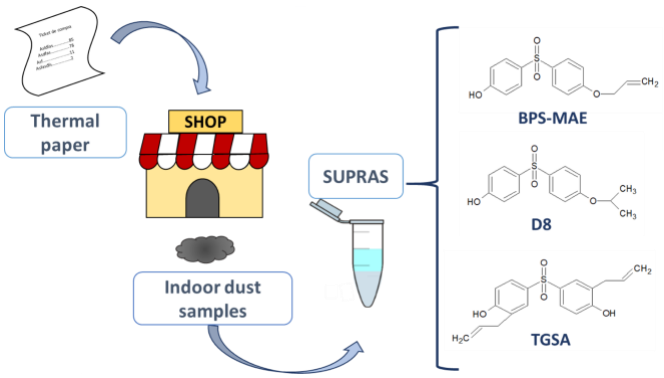


Highlights

- A SUPRAS microextraction was optimized for generic treatment of bisphenols in dust.
- Targets were BPA, BPS, BPF, BPS-MAE, D8 and TGSA (color developers in thermal paper).
- Dust was collected from public microenvironments with frequent use of thermal paper.
- BPS-MAE, D8 and TGSA were frequently detected in dust (50-90%) at 6 – 22 ng $\cdot g^{-1}$.

Abstract

Bisphenol A (BPA) is present in a wide variety of materials and it is a well-known endocrine disruptor that is widespread in the indoor and outdoor environment. For this reason, industry has introduced a variety of replacements, such as Bisphenol S (BPS) or Bisphenol F (BPF), and other less known structural analogs, such as BPS-MAE, D-8 or TGSA. These emerging potential contaminants have been identified in thermal paper products, according to recent studies, but their potential toxic effects and their migration into the environment it is still unclear. In this study, we report for the first time the presence of these emerging BPA replacements in indoor dust from public environments (shops, restaurants, etc.). For this purpose, we optimized a novel supramolecular solvent (SUPRAS)-based microextraction method. SUPRAS are multi-target solvents made up of self-assembled amphiphiles. They offer multiple extraction interactions (dispersion, polar, hydrophobic, etc.) and constitute excellent candidates to develop generic and fast sample treatment procedures at low cost. By this method, emerging BPA replacements (BPS-MAE, D-8 and TGSA) were detected in dust at median concentrations in the range 6 – 22 $ng \cdot g^{-1}$ (around ten times lower than BPS) with detection frequencies in the range 50 – 90%. These results constitute a first insight into the migration of emerging BPA replacements into the environment via indoor dust, which is a common route of human exposure to contaminants.

Keywords: *supramolecular solvents, indoor dust, bisphenol A, bisphenol S, BPS-MAE, D-8, TGSA.*

1. Introduction.

Bisphenol A (BPA) or 4,4'-(propane-2,2-diyl)diphenol, is used worldwide and its production volume is one of the highest in the industry. It is used in wide variety of applications from food-related plastics (food-packaging, bottles, cookware, tableware, etc.) to other materials, such as medical devices, printing inks, thermal paper, etc. BPA can migrate into the environment because plastic contains non-polymerized monomer residues or because it is released by ester bonds hydrolysis under heat or reaction with the acid or basic contents of the bottles (Björnsdotter et al., 2017a). BPA has become an ubiquitous environmental contaminant, which is present in river waters (1.0 – 628 ng $\cdot L^{-1}$) (Suzuki et al.,2004; Ballesteros-Gómez et al., 2007; Ruiz et al., 2007; Yamazaki et al., 2015), sediments (3.94 – 2.2 $\cdot 10^{6}$ ng $\cdot g^{-1}$ d.w.) (Terasaki et al., 2007; Liao et al., 2012a; Wang et al., 2016), sewage sludge (0.42 – 25,600 ng $\cdot g^{-1}$) (Song et al., 2014; Lee et al., 2015; Yu et al., 2015), air (indoor: <0.1 – 1.8 ng $\cdot m^{-3}$, outdoor: <0.1 – 2.5 ng $\cdot m^{-3}$) (Wilson et al., 2001) and dust (535 – 9,730 ng $\cdot g^{-1}$) (Geens et al., 2009). It has also been widely detected in biological samples, such as blood (0.79 – 7.12 ng $\cdot mL^{-1}$) (Owczarek et al., 2018) saliva (mean of 3.64 µg $\cdot L^{-1}$) (Lee et al., 2017) or urine (mean of 2.6 µg $\cdot L^{-1}$) (Casas et al., 2013). BPA is a well-known endocrine disruptor (Rochester, 2011), it is capable to disrupt the thyroid hormone action, affecting vertebrate development (Zhang et al., 2017) and it can act as neurodevelopmental toxicant too (Kincha et al., 2015).

In order to evade regulatory oversight and social pressure, industry has introduced BPA replacements into the market. Replacements are usually structural analogs to BPA with similar physicochemical properties and, subsequently, similar potential toxicity (Gramec Skledar and Peterlin Masic, 2016; Russo et al., 2018). Bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol AF (BPAF), bisphenol E (BPE), tetrabromobisphenol A (TBBPA), bisphenol A diglycidyl ether (BADGE) and bisphenol F diglycidyl ether (BFDGE) are common BPA replacements. They are used in a variety of materials too, such as electronic equipment,

cans' lacquer coating, dental sealants and flame retarded products (Björnsdotter et al., 2017a). Due to this massive utilization, they have also been widely reported in sediments (3.2 – 12.6 ng·g^{-1}), sewage sludge (12.8 – 4,730 ng·g^{-1}) or indoor dust (0.15 – 4.18 µg·g^{-1}), etc. (sum of all detectable analogues including BPA) (Chen et al., 2016).

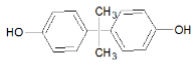
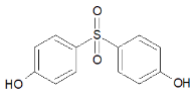
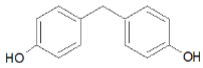
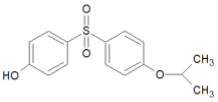
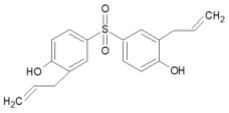
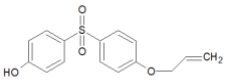
Other widespread use of BPA is thermal paper (Geens et al., 2012; Björnsdotter et al., 2017a; Pivnenko, 2018). Replacements have also been introduced into the market for this aim, namely BPS and other less known compounds such as 4-hydroxyphenyl 4-isopropoxyphenyl Sulfone (D-8), 4,4′-sulfonylbis(2-allylphenol) (TGSA), 4-((4-(allyloxy)phenyl)sulfonyl)phenol (BPS-MAE), Pergafast 201 and D-90 (US EPA, 2015). Although there are some recent studies about the presence of these compounds in thermal paper products and their potential toxic effects (Goldinger et al. 2015; Björnsdotter et al., 2017b; Eckardt and Simat, 2017) their migration and presence in the environment have not been assessed so far.

Indoor dust is a potential source of human exposure to BPA and its analogs due to their migration from many materials and slow degradation (Rudel et al., 2003; Völkel et al., 2008; Geens et al., 2011 and 2012). Concentration values in indoor dust usually range from ng·g^{-1} to µg·g^{-1} levels. Levels up to 39,000 ng·g^{-1} of BPA and up to 26,600 of BPS ng·g^{-1} have been reported in different countries from US and Asia (Liao et al. 2012b; Wang et al. 2015). In the present study, BPA replacements used in thermal paper (BPF, BPS, BPS-MAE, D-8, TGSA) (Table 1) were analyzed in indoor dust for the first time.

To carry out the study, a novel simultaneous extraction/clean-up method based on the use of supramolecular solvents (SUPRASs) was optimized. SUPRASs are nanostructured liquids produced from self-assembled amphiphilic compounds (Caballo et al., 2017; Ballesteros-Gómez et al., 2018). They are excellent extraction materials that offer multiple binding interactions (ionic, anionic, hydrogen bonds, dispersion

interactions, etc.).

Table 1. Compound name and CAS number, molecular structure, chemical formula, monoisotopic mass and log P of BPA, BPS, BPF, BPS-MAE, D-8 and TGSA.

Compound & CAS	Molecular structure	Chemical formula	Monoisotopic mass (g/mol)	Log P
4,4'-(propane-2,2-diyl) diphenol (BPA) ***80-05-7***		$C_{15}H_{16}O_2$	228.115	3.32[a] 3.3[b]
4,4´-Sulfonyldiphenol (BPS) ***80-09-1***		$C_{12}H_{10}O_4$	250.030	1.9[b]
4,4'-Methylenediphenol (BPF) ***620-92-8***		$C_{13}H_{12}O_2$	200.084	2.91[a] 2.9[b]
4-(4-propan-2-yloxyphenyl) sulfonylphenol (D-8) ***95235-30-6***		$C_{15}H_{16}O_4S$	292.077	3[b]
4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (TGSA) ***41481-66-7***		$C_{18}H_{18}O_4S$	330.093	4.1[b]
4-(4-phenylmethoxyphenyl) sulfonylphenol (BPS-MAE) ***63134-33-8***		$C_{19}H_{16}O_4S$	340.077	4.2[b]

Binding interactions can be adjusted for each purpose by switching the functional groups of the amphiphile and the nature of the coacervation-inducing agent (Caballo et al., 2017; Ballesteros-Gómez et al., 2018). Their nanostructure give rise to microenvironments of different polarity and confer them restricted access properties for the exclusion of macromolecules, which are common interferents in analytical applications (Ballesteros-Gómez et al., 2012). Further advantages are their easy synthetic procedures, non-volatility and non-flammability (Caballo et al., 2017; Ballesteros-Gómez et al., 2018). All these properties make them

excellent candidates for generic sample treatment of indoor dust, a complex and heterogeneous matrix containing from textile and paper fibers to human or animal hair, cells and mineral components, among others. Dust samples were collected in public environments, because of the frequent use of thermal paper cash receipts. Results constitute a first insight into the possible migration of these contaminants into the environment.

2. Materials and methods.

2.1. Chemicals and reagents.

All solvents were of analytical reagent-grade and were used as supplied. Methanol (MeOH) and tetrahydrofuran (THF) were acquired from VWR – Prolabo Chemicals (Bois, France). 1- Octanol and 1- Decanol, were obtained from Sigma-Aldrich (St. Louis, MO, USA), while 1- Hexanol was supplied by Merck (Darmstadt, Germany). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain).

A standard reference material (SRM) Trace Metals - Baghouse Dust was used for optimization and validation purposes. It was purchased from Sigma-Aldrich (St. Louis, MO, USA). The target compounds: 4,4'-(propane-2,2-diyl) diphenol (bisphenol A, BPA), 4,4'-Sulfonyldiphenol (bisphenol S, BPS) and 4,4´-Methylenediphenol (bisphenol F, BPF) were acquired from Sigma-Aldrich (St. Louis, MO, USA). 4-(4-propan-2-yloxyphenyl) sulfonylphenol (D-8), 4-(4-hydroxy-3-prop-2-enylphenyl) sulfonyl-2-prop-2-enylphenol (TGSA) and 4-(4-phenylmethoxyphenyl) sulfonylphenol (BPS-MAE) were obtained from Toronto Research Chemicals (Toronto, Canada). The internal standards (IS) Bisphenol A-d_6 diglycidyl Ether (BPA-d_6) and bis(4-hydroxyphenyl) Sulfone-d_8 (BPS-d_8) were also obtained from Toronto Research Chemicals.

Stock solutions of individual bisphenols (2 mg·mL^{-1}) were prepared in MeOH and stored at -20ºC. A spike solution of internal standards (BPS-d_8 and BPA-d_6) was prepared in MeOH at a concentration of 5 mg·L^{-1} for optimization and for sample analysis. Intermediate and working solutions of bisphenols and of internal standards mixtures were prepared by appropriate dilution in MeOH and stored at -20ºC.

2.2. Apparatus.

The analysis was carried out using an Agilent Technologies 1200 LC system with a column Phenomenex Luna® C_8 column (2.0 mm i.d., 100 mm length, 3.0 μm particle size) preceded by a precolumn Phenomenex KJ 0-4282 SecurityGuard Cartridge Kit, Ea. This was coupled to an Agilent Technologies 6420 Triple Quadrupole mass spectrometer equipped with an electrospray ionization (ESI) source operating in negative mode. An additional LC column (Agilent Eclipse Plus C8 5 μm, 4.6 mm × 50 mm) was inserted between the pump and injector in order to trap possible bisphenols released from the instrument. Raw data was controlled and processed using Agilent MassHunter Software® (version B.07.00).

Other instrumentation used for sample preparation were a vortex-shaker REAX Top (Heidolph, Schwabach, Germany) and a 12 x 1.5 – 2 mL angle rotor Minicen centrifuge from Ortoalresa (Madrid, Spain).

2.3. SUPRAS method optimization.

Optimization of SUPRAS was carried out by extraction of a mix dust (collected in two houses in Córdoba, sieved to 0.5 mm and homogenized), fortified at 5,000 ng·g^{-1} (BPA, BPF, BPS, D-8 and TGSA) and of internal standards (BPS-d_8 and BPA-d_6).

Dust aliquots (50 mg) were added to 2 mL Eppendorf microtubes, followed by SUPRAS synthetic solutions (120 – 200 μL of amphiphile and

a mixture of water:THF up to 1.2 mL). Samples were vortex-stirred for 5 min for SUPRAS formation, sample dispersion and extraction, and centrifuged for 20 min at 10,000 rpm for phase separation. At the end, three phases were observed: SUPRAS (upper phase), equilibrium solution (in the middle, containing water:THF and a residual amount of amphiphile at the critical aggregation concentration) and the solid matrix (at the bottom). The SUPRAS phase, enriched with the target compounds, was diluted to 1 mL with MeOH to facilitate the optimization process by keeping constant the final volume and aliquots of 3 µL were directly injected into the LC-MS/MS system.

Both the final composition and microstructure characteristics of the SUPRAS depend on the nature and composition of the initial synthetic solution. A variety of SUPRAS were generated with different amphiphiles and by tuning the composition of the initial ternary mixture (amphiphile:water:THF) and tested for extraction. The following experimental conditions were studied: type of amphiphile (1-hexanol, 1-octanol and 1-decanol), concentration of amphiphile (10 – 16.67, % v/v) and concentration of THF (8.33 – 33.33, % v/v) for a final volume of 1.2 mL. Experiments were made in triplicate. Optimal conditions were selected on the basis of extraction efficiency and concentration factor [SUPRAS volume (µL)/ sample size (mg)].

2.4. SUPRAS method validation.

The linearity, detection and quantitation limits and matrix effects of the method were assessed by running calibration with two dust samples, i.e. the in-house dust mix and the SRM Trace Metals - Baghouse Dust, and at two sample sizes (25 and 50 mg). Results were compared with those obtained from SUPRAS calibration. The optimal SUPRAS (synthetic conditions: 200 µL 1-hexanol, 200 µL THF, 800 µL water) was applied to dust samples fortified in the range 10 – 10,000 ng·g^{-1} of the target compounds and 5,000 ng·g^{-1} of IS mix (mix of BPA-d_6 and BPS-d_8 at 5 mg·L^{-}

[1]). Unfortified SUPRAS (blanks) and dust samples were also analysed (in triplicate). Levels of target compounds were below LODs in the blanks and in the two dust samples.

The limits of detection (LOD) and quantification (LOQ) (ng $\cdot g^{-1}$) of the method were estimated from a signal-to-noise ratio of 3 and 10, respectively.

2.5. Analysis of bisphenols.

2.5.1. Sample collection.

Sampling was performed using a vacuum cleaner with bags. Samples were collected in Spain in 2018 from public environments (n=10): two electronic shops, two clothing shops, one sport clothing shop, one decoration shop, three bazaars and one cafeteria. Samples were homogenized and sieved to 0.5 mm.

2.5.2. Hexanol - based SUPRAS extraction.

First, approximately an aliquot of 25 mg of dust was weighed in a 2 mL Eppendorf microtube. The SUPRAS synthetic solution (200 µL of hexanol, 200 µL of THF and 800 µL of water) was added and spiked with 25µL of IS mix. SUPRAS formation and microextraction/clean-up was performed in a single-step by vortexing (5 min) and centrifugation at 10,000 rpm for 20 min. After phase-separation, 150 µL of SUPRAS (the top layer) was collected, transferred to an LC vial and aliquots of 3 µL measured by LC MS/MS. A schema is shown in Figure 1.

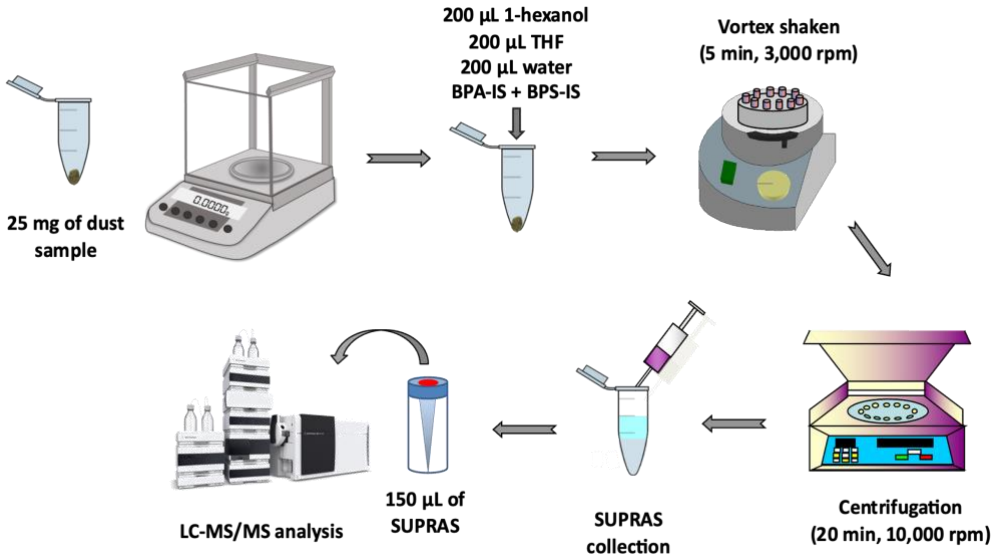


Figure 1. *Schema of SUPRAS method for the determination of emerging BPA replacements in indoor dust samples.*

2.5.3. Quantification of bisphenols by LC – MS/MS.

The mobile phase was made up of Milli-Q water (A) and MeOH (B) at a flow rate of 0.25 mL·min^{-1}. The injection volume was 3 µL. The gradient was as follow: initial 100% A hold for 1 min and decreased to 30% in 5 min, holding for 7 min, increased B to 100% and maintained for 6 min and finally re-conditioning for 7 min.

The MRM transitions for target masses are given in Table 2. BPA, BPF, BPS, BPS-MAE, D-8 and TGSA were analyzed in ESI negative ionization mode. The optimal source parameters were: gas temperature, 300 °C; gas flow, 11.0 L·min^{-1}; nebulizer gas pressure, 15 psi; capillary voltage, -4500 V; MS1 heater, 100 °C; MS2 heater, 100 °C.

Quantitative analysis MassHunter workstation software from Agilent Technologies was used for quantification of bisphenols. Calibration was performed with SUPRAS in the range 10 – 10,000 ng·g^{-1}

and by using the deuterated internal standard BPA-d_6, except for BPS, for which BPS-d_8 was used instead (at a final concentration of 5,000 ng $\cdot g^{-1}$).

Table 2. MRM transitions, dwell time, fragmentor voltage and collision energy. Quantifiers for target compounds are indicated in bold

Compound	Precursor ion (m/z)	Product ion (m/z)	Dwell time (ms)	Fragmentor (V)	Collision energy (eV)	Polarity
BPA	**227.1**	**212.2**	**50**	**100**	**20**	Negative
BPA	227.1	113.0	50	100	24	Negative
BPF	**199.0**	**105.0**	**50**	**100**	**25**	Negative
BPF	199.0	93.0	50	100	30	Negative
BPS	**249.0**	**108.0**	**50**	**100**	**20**	Negative
BPS	249.0	92.1	50	100	32	Negative
BPS-MAE	**289.1**	**248.1**	**50**	**100**	**20**	Negative
BPS-MAE	289.1	184.1	50	100	30	Negative
D8	**291.1**	**248.0**	**50**	**100**	**25**	Negative
D8	291.1	184.1	50	100	25	Negative
TGSA	**329.1**	**132.1**	**50**	**100**	**25**	Negative
TGSA	329.1	148.1	50	100	25	Negative

3. Results and discussion.

SUPRASs have been already successfully applied in the extraction of bisphenols from food (Ballesteros-Gómez et al., 2009), urine (García-Prieto et al. 2008; Salatti-Dorado et al., 2016), environmental waters and wastewaters (Ballesteros Gómez et al., 2007), etc. SUPRASs are generated in a self-assembly and coacervation process that occurs on two scales (Caballo et al., 2017; Ballesteros-Gómez et al., 2018). First, amphiphiles form tridimensional aggregates (mainly micelles and/or vesicles) in solution. Then, aggregates self-assemble into a new highly packed phase (SUPRAS) by the stimuli of a coacervation-inducing agent (change of pH,

temperature, addition of salt or addition of a poor solvent for the amphiphile). They are very tunable solvents whose composition and micro- or nano-structure change with the nature and composition of the synthetic solution (Ballesteros-Gómez et al., 2012; Ballesteros-Gómez et al., 2018).Both aspects influence recoveries of the target compounds and the simultaneous exclusion of interferents (usually macromolecules or polymers which are non-soluble in the SUPRAS medium or which are size-excluded due to the limited pore size of the SUPRAS network). In general, amphiphiles with longer alkyl chain length give rise to more hydrophobic SUPRAS, which have less content in water and which also provide less energetic hydrogen bonds for extraction. Furthermore, SUPRAS with higher content in water produce bigger coacervate droplets and less packed structures. This usually results in better extraction efficiency for polar and moderate polar compounds, such as bisphenols (Salatti-Dorado et al., 2016; Ballesteros-Gómez et al., 2018). Phase diagrams (for SUPRAS formation) and composition of SUPRAS made up of inverse aggregates of 1-hexanol in THF:water have been recently reported by our group and they have been proven to be suitable for the extraction of BPA (Salatti-Dorado et al., 2016). For this reason they were selected for the study of novel BPA replacements. SUPRAS formation just requires mixing and centrifuging the synthetic solution for accelerating phase separation. Then, we observed two phases: the aqueous equilibrium solution at the bottom (containing the residual alcohol at a low critical micellar concentration) and the SUPRAS phase containing the majority of the amphiphile packed as an inverse hexagonal phase. Figure 2 shows a schema of the SUPRAS formation and its structure. The equilibrium solution helped to disperse the sample and favored the extraction process at such a low volume of SUPRAS phase (usually 100 – 500 μL). Furthermore, it acts as sink of polar interferents.

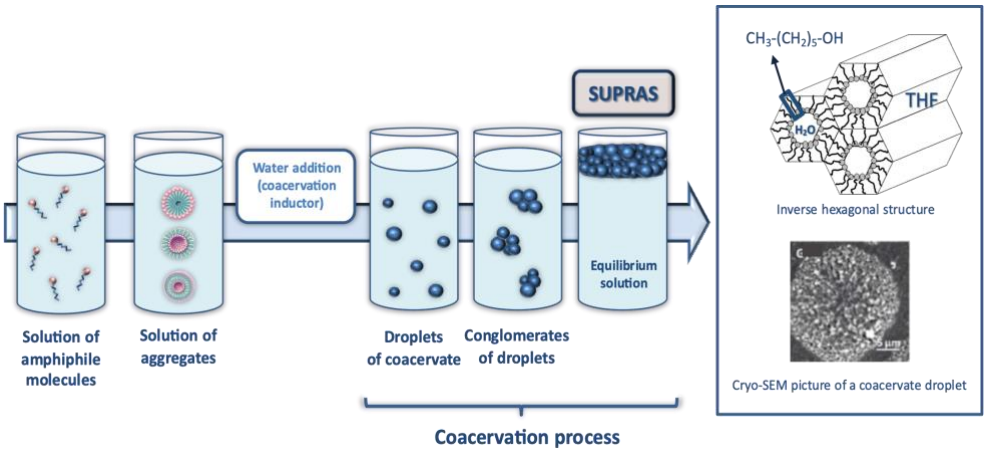
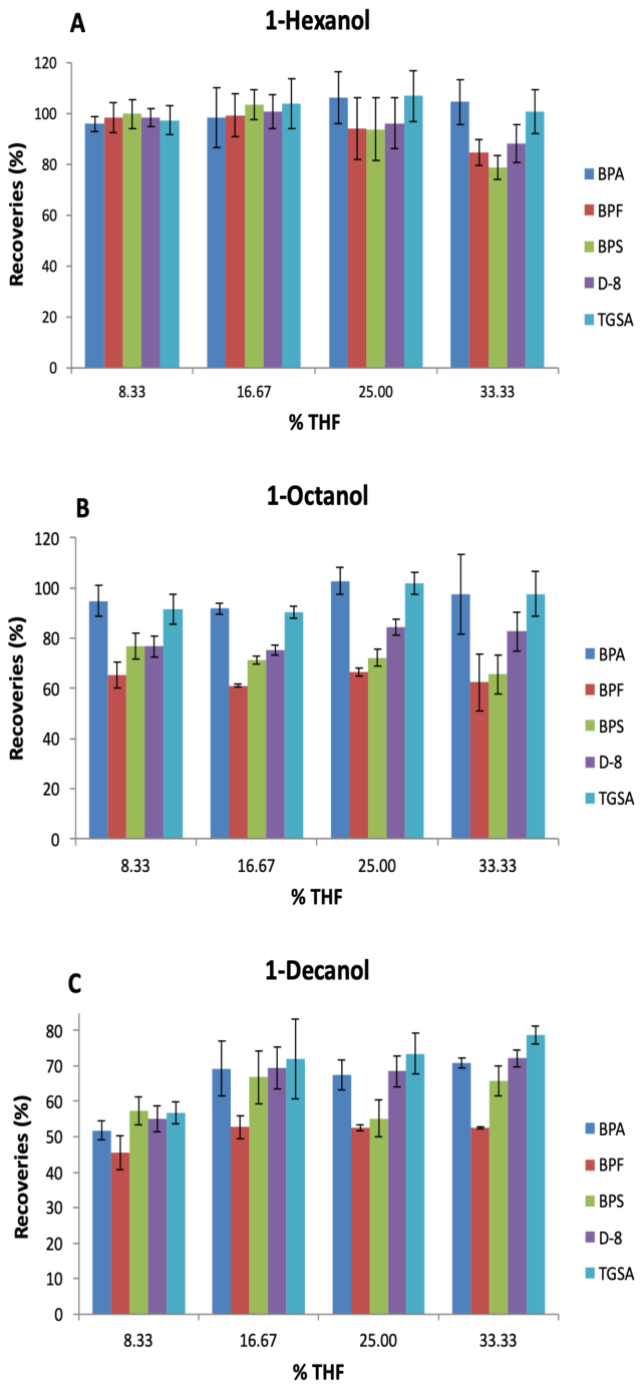


Figure 2. *Schema of the synthesis of the SUPRAS made up of 1-hexanol in THF:water mixtures, which involves processes of self-assembly and coacervation.*

3.1. SUPRAS optimization.

As preliminary experiments, SUPRAS blanks (without dust) were underwent extraction by changing the type of amphiphile (1-hexanol, 1-octanol and 1-decanol, in a range of 10 – 16.67, % v/v) under different percentages of THF (8.33, 16.67, 25 and 33.33, % v/v) in order to establish the recovery of the target compounds against the equilibrium solution. Figure 3 shows the recoveries of analytes (BPA, BPF, BPS, BPS-MAE, D-8 and TGSA) for each amphiphile using 120 µL of amphiphile (10% v/v). Considering the alkyl chain length, recoveries decreased with an increasing number of carbon atoms. Although 1-octanol had similar recoveries than 1-hexanol for some analytes, the latter provided good extraction efficiency in a wider polarity range. The higher recoveries with SUPRAS of shorter alkyl-chain length amphiphiles can be attributed to both strongest hydrogen bonds for extraction, as explained above, and smaller aggregate sizes offering a higher contact surface for binding the contaminants. As shown in Figure 3, the percentage of THF did not influence recoveries so significantly in the tested range.



SUPRAS volumes increased exponentially with the THF percentage (see Table S1), so that the concentration factor also dropped.

For this reason, an intermediate value of 16.67% v/v THF was set as optimal for further experiments.

Once the optimal amphiphile and THF percentages were selected, we evaluated different volumes of 1-hexanol to form the SUPRAS. Recoveries were expected to increase with the percentage of amphiphile and concentration factors to decrease linearly (as SUPRAS volumes

Figure 3. *Extraction efficiency of target compounds with SUPRAS based on amphiphiles of different alkyl chain length (C6, C8 and C10) under different percentages of THF and expressed as mean ± SD (n=3). Conditions: blanks (dust: 0 mg), concentration of amphiphile (10% v/v), concentration of THF (8.33 – 33.33, % v/v), final volume of 1.2 mL.*

increased). Experiments were carried out in the presence of dust (50 mg) with SUPRASs formed with 120, 150 and 200 µL of amphiphile (10, 12.5 and 16.67% v/v, respectively). Recoveries were maximal with 200 µL of 1-hexanol and were of 93 ± 3 for BPA, 77 ± 4 for BPS, 88 ± 2 for BPF, 80 ± 2 for D-8 and 82 ± 3 for TGSA. These values were just slightly lower than without dust at the same 1-hexanol percentage (see figure S1).

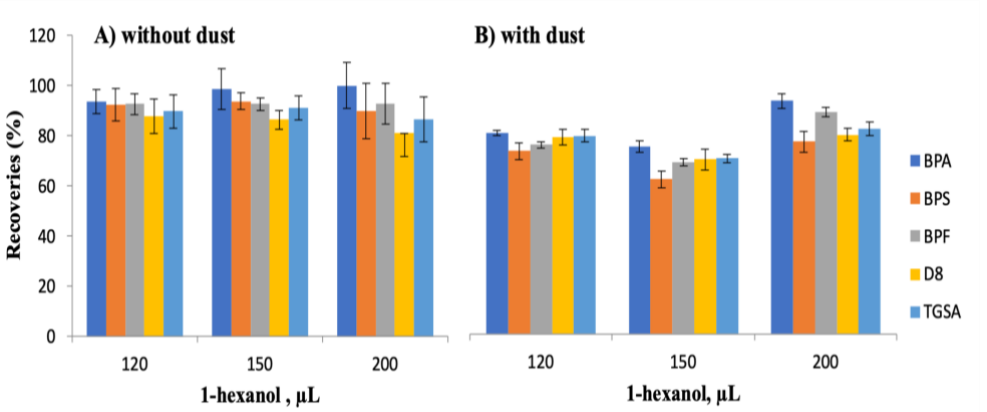


Figure S1. *Recoveries with standard deviations (n=3) of target compounds with SUPRAS made up of different volumes of 1-hexanol and ~17% v/v THF without and with the presence of the matrix (50 mg of indoor dust).*

Under these conditions the SUPRAS volume extract was of 207 µL (calculated as specified in Table S1).

Table S1. Volumes of SUPRASs (µL) synthesized with different percentages of tetrahydrofuran and 120 uL (10% v/v) of amphiphile

	Amphiphiles		
THF, %v/v	**[a]1-Hexanol**	**[b]1-Octanol**	**[b]1-Decanol**
8.33	154	163	164
16.67	207	232	234
25.00	277	334	337
33.33	373	485	489

[a]Calculated as: $V_{SUPRAS} = (10.7 \pm 0.3) \cdot H \cdot e^{(0.0330 \pm 0.0007) \cdot THF}$; where H and THF were 1-hexanol and THF percentages in the bulk solution, respectively (Salatti-Dorado et al., 2016).

[b]Calculated as $V_{SUPRAS} = X \cdot [A + e^{BZ}]$; where A= 0.17 ± 0.02; B= 0.03389 ± 0.0003; X= amount of alkanol in mg and Z= THF percentage (v/v) in the THF:water mixture in the bulk solution (Ballesteros-Gómez, A and Rubio, S. 2012).

3.2. Analytical performance and validation.

Calibration curves were prepared in SUPRAS (10 – 10,000 ng·g^{-1}, *n*=11, 5,000 ng·g^{-1} of IS mix). As can be seen in Table 3, the correlation coefficients were in the range 0.9597 – 0.9993. Method detection (MDL) and quantification (MQL) limits were estimated considering a signal to noise ratio of 3 and 10, respectively, and were in the range 0.5 – 10 and 1 – 20 ng·g^{-1}, respectively.

Table 3. Analytical performance of the SUPRAS-based calibration[a]

	Slope (ua g · ng^{-1}) ± Error	Lineal range (ng·g^{-1})	R^2	LOD (ng·g^{-1})	LOQ (ng·g^{-1})
BPA	0.000151 ± 3·10^{-6}	20-10,000	0.9977	10	20
BPS	0.0020 ± 0.0001	2-10,000	0.9872	1	2
BPF	0.000081 ± 2·10^{-6}	20-10,000	0.9962	10	20
D8	0.012 ± 0.001	2-10,000	0.9597	1	2
TGSA	0.0015 ± 0.0001	2-10,000	0.9759	1	2
BPS-MAE	0.00309 ± 3·10^{-5}	1-10,000	0.9993	0.5	1

[a]*IS mix at 5,000 ng/g, n=11, weight 1/x, origin included*

Calibration curves were also run in the presence of two dust samples (mix dust and SRM Baghouse dust) at two sample sizes (25 and 50 mg) to validate the methodology at the same spiking levels (10 – 10,000 ng·g^{-1}, *n*=11). Matrix effects were calculated as the ratio from both slopes ($SUPRAS_{with\ dust}$/SUPRAS x 100) and were acceptable and in the ranges 70 – 100% and 86-120% for the dust mix and the SRM, respectively, at 25 mg, so that this sample size was considered as optimal. Correlation coefficients were in the range 0.9651 – 0.9961 and 0.9915 – 0.9995 for the dust mix and the SRM, respectively. SUPRAS blanks and unfortified dust samples did not contain detectable levels of the target compounds.

3.3. Extraction of bisphenols in real samples.

Ten indoor dust samples collected from different public environments and they were analyzed by the validated SUPRAS method. Table 4 shows the concentration range, mean, median and detection percentages for each analyte.

Table 4. Concentration of target compounds (in ng·g^{-1}) found in indoor dust samples from different public microenvironment in Spain (n=10)

	BPA	BPF	BPS	BPS-MAE	D8	TGSA
Concentration range	192-4444	Detected - 183	n.d.-736	n.d.-79	n.d.-58	n.d.-48
Mean[a]	1883	79	290	20	23	22
Median[b]	1739	60	193	6	20	22
Detection percentage (%)	100	100	70	50	70	90

n.d.: non-detected

[a]: Calculated without values below the LOQ

[b]: Calculated without values below the LOQ

In Table S2 the concentrations of the target compounds and the IS recoveries in each sample is specified. IS recoveries varied in the ranges 71 – 108 and 69 – 95% for BPA-d_6 and BPS-d_8, respectively. BPA was the most abundant bisphenol detected in all the samples, with a mean of 1,883 ng·g^{-1} followed by BPS (203 ng·g^{-1}) and BPF (70 ng·g^{-1}), which are their most used analogs in the industry. These concentrations are well in agreement with those reported in other countries (see Table S3). For example, concentrations for BPA in the literature ranges from 630 to 3,260 ng·g^{-1} (median) (Liao et al., 2012) and from 100 to 3,800 ng·g^{-1} (mean) (Wang et al., 2015); for BPF ranges from 38 to 450 ng·g^{-1} (median) (Liao et al., 2012) and from 1.9 to 5,500 ng·g^{-1} (mean) (Wang et al., 2015) and for BPS ranges from 170 to 810 ng·g^{-1} (median) (Liao et al., 2012) and from <2 to 1,500 ng·g^{-1} (mean) (Wang et al., 2015). In this study levels were in

the ranges 192 – 4,444 ng·g^{-1}, 29 – 183 ng·g^{-1} and <0.075 – 736 ng·g^{-1} for BPA, BPS and BPF, respectively.

Emerging BPA replacements (BPS-MAE, D-8 and TGSA), which are for the first time reported in this study, were detected in 50%, 70% and 90% of the dust samples, respectively. They were less abundant than BPS and BPF, with medians between 6 and 22 ng·g^{-1} (around ten-fold lower values). This suggests that they are used in lower amounts or in fewer types of materials or that their migration is slower than that of the other bisphenols. We could not find information about other uses than thermal paper.

Table S2. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different public microenvironments and recoveries of internal standards

	Concentrations						Recoveries	
	BPA	BPF	BPS	BPS-MAE	D-8	TGSA	BPA-d_6	BPS-d_8
Electronic shop 1	4444.2	41.3	193.1	79.2	34.5	21.8	82.6	88.6
Electronic shop 2	1523.3	Detected	113.1	n.d.	10.2	23.2	83.0	93.9
Clothing shop 1	2262.6	30.7	162.9	n.d.	10.4	<LOQ	86.4	83.7
Clothing shop 2	1953.9	Detected	173.3	7.2	22.0	39.8	96.5	93.2
Sport clothing shop	2308.2	45.6	735.9	3.9	20.2	8.5	108.1	94.4
Decoration shop	4231.8	100.8	342.6	6.0	58.3	48.2	78.1	73.8
Cafeteria	791.2	183.1	307.0	n.d.	n.d.	n.d.	101.3	94.3
Bazaar 1	533.9	74.4	n.d.	n.d.	n.d.	<LOQ	72.8	88.5
Bazaar 2	192.1	118.3	n.d.	n.d.	n.d.	2.4	70.7	69.0
Bazaar 3	589.1	35.8	n.d.	2.4	6.5	9.9	106.9	94.7

n.d.: non-detected

Table S3. Concentrations (in ng·g^{-1}) of some bisphenols (bisphenol A, bisphenol F and bisphenol S) found in indoor dust from several countries

	Liao et al., 2012[a]			Wang et al., 2015[b]		
Countries	**BPA**	**BPF**	**BPS**	**BPA**	**BPF**	**BPS**
U.S	1600	49	630	3800	4400	2.1
China	630	38	170	670	1.9	<2
Japan	2700	57	810	2800	650	440
Korea	3260	450	360	1100	1300	8.8
Colombia	-	-	-	420	69	3.7
Greece	-	-	-	1700	5500	1500
India	-	-	-	360	29	12
Kuwait	-	-	-	390	78	38
Pakistan	-	-	-	100	56	10
Romania	-	-	-	680	41	380
Saudi Arabia	-	-	-	1100	160	110
Vietnam	-	-	-	330	200	28

[a]*median values,* [b]*mean values*

4. Conclusions.

The emerging BPA replacements (BPS-MAE, D-8 and TGSA) were detected for the first time in indoor dust, at median levels around ten times lower than BPS but frequently detected (50 – 90%). These replacements have previously been reported as colour developers in thermal paper. The SUPRAS method is suitable as generic sample treatment of indoor dust, the procedure was simple and fast (5 min stirring + 20 min centrifugation), recoveries were within the required levels (69 – 108%) and LODs were satisfactory for this matrix (in the low ng·g^{-1}). Results show the potential of these emerging contaminants to migrate into the environment and constitute a first insight into their presence in indoor dust as a relevant route of exposure. It is worthy to monitor these compounds in future studies taken into account the limited number of samples and the fact that they seems to be frequently present, specially taken into account that they are considered toxic (TGSA, D-8) and very toxic (BPS-MAE) to aquatic life according to the data available on the ECHA database.

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Emerging contaminatns
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Emerging bisphenol A replacements (colour developers) in indoor dust from Spain

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Abstract

Bisphenol A (BPA) and replacements, such as bisphenol S (BPS) and F (BPF) and other substitutes (BPS-MAE, D-8 and TGSA) have been recently reported in thermal paper. In this study, BPA, BPS, BPF, BPS-MAE, D-8 and TGSA were analysed in indoor dust collected in Spain from different microenvironments (living rooms, bedrooms, cars and offices). Levels were compared with those reported in our previous study (shops and other public microenvironments, where frequent use of thermal paper is expected). We investigated the differences between microenvironments, possible correlations between compounds and estimated the ingestion rates. BPS-MAE, D-8 and TGSA were present at levels up to 529, 128 and 356 ng·g^{-1}, respectively, in all the microenvironments. The highest levels were measured in cars.

Keywords: *bisphenol A, bisphenol F, bisphenol S, BPS-MAE, D-8, TGSA, indoor dust.*

1. Introduction

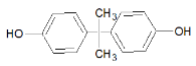
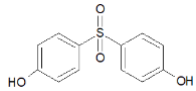
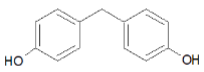
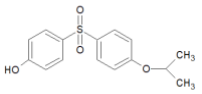
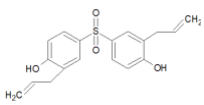
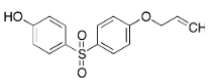
Indoor dust is a recognized source of exposure to organic contaminants. Dust contains high levels of contamination (up to mg·g^{-1}) because of the migration of compounds from materials and their slow degradation [1-4]. Children are particularly exposed and ingest a higher amount of dust than adults due to frequent hand-to-mouth and object-to-mouth activities. Among indoor dust contaminants, bisphenol A (BPA) and analogs are frequently detected, since they are used worldwide in many products (e.g. food-related material, finishing products, electronic equipment, thermal paper, etc.). BPA, BPS and BPF have been reported up to 39,100 ng·g^{-1}, 26,600 ng·g^{-1} and 107,000 ng·g^{-1}, respectively, in dust samples of several European, Asian and American countries [5,6].

However, the presence of BPA analogs employed as color developers in thermal paper has been scarcely investigated, such as 4-hydroxyphenyl 4-isopropoxyphenyl Sulfone (D8), 4-(4-(allyloxy)phenyl)sulfonyl)phenol (BPS-MAE) and 4,4′-sulfonylbis(2-allylphenol) (TGSA) [7-10]. Recently, these compounds and other BPA replacements (e.g. Pergafast 201, D-90) have been reported in thermal paper [7-10]. Studies show that they are already widely used despite the lack of current restrictive legislation of BPA in thermal paper. Their use is expected to increase in the future since the EU has established a limit of 0.02% of BPA in thermal paper after January 2020 [11].

Although handling thermal paper has been identified as a source of exposure to BPA alternatives [12, 13], dust ingestion should be assessed too as an additional source of exposure. To the best of our knowledge, the presence of these compounds in dust has only been reported in samples of public microenvironments in a previous study of our group [14]. We analyzed ten samples of indoor dust from different shops, cafeterias and bazaars, where there is a frequent use of thermal paper. We found levels of BPS-MAE, D-8 and TGSA up to 79, 58 and 48 ng·g^{-1} with detection frequencies of 50, 70 and 90%, respectively, this proving their ability to

migrate into the environment. In this study, we analyze these three emerging replacements together with BPA, BPS and BPF in other microenvironments (living rooms, bedrooms, cars and offices). We investigate differences between microenvironments, correlations between compounds and estimate exposure levels in order to evaluate the risk for the human health. Table 1 shows the structure, formula, CAS and monoisotopic mass of the compounds analyzed in this study.

Table 1. Target compounds: structure, formula, CAS and monoisotopic mass

Compound & CAS	Molecular structure	Chemical formula	Monoisotopic mass (g/mol)
4,4'-(propane-2,2-diyl) diphenol (BPA) ***80-05-7***		$C_{15}H_{16}O_2$	228.115
4,4´-Sulfonyldiphenol (BPS) ***80-09-1***		$C_{12}H_{10}O_4$	250.030
4,4'-Methylenediphenol (BPF) ***620-92-8***		$C_{13}H_{12}O_2$	200.084
4-(4-propan-2-yloxyphenyl) sulfonylphenol (D-8) ***95235-30-6***		$C_{15}H_{16}O_4S$	292.077
4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (TGSA) ***41481-66-7***		$C_{18}H_{18}O_4S$	330.093
4-[4-(prop-2-en-1-yloxy)benzenesulfonyl] phenol(BPS-MAE) ***97042-18-7***		$C_{15}H_{14}O_4S$	340.077

2. Experimental section

2.1. Chemicals and reagents

All solvents were of analytical reagent-grade and they were used as supplied. Methanol (MeOH) and tetrahydrofuran (THF) were obtained from VWR – Prolabo Chemicals (Bois, France). 1-Hexanol was supplied by Merck (Darmstadt, Germany). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain).

A standard reference material (SRM) Trace Metals - Baghouse Dust, with number CRM014, was used for optimization and validation purposes and was purchased from Sigma-Aldrich (St. Louis, MO, USA).

The target compounds: 4,4'-(propane-2,2-diyl) diphenol (bisphenol A, BPA), 4,4´-Methylenediphenol (bisphenol F, BPF) and 4,4´-Sulfonyldiphenol (bisphenol S, BPS) were obtained from Sigma-Aldrich (St. Louis, MO, USA). 4-(4-phenylmethoxyphenyl)sulfonylphenol (BPS-MAE), 4-(4-propan-2-yloxyphenyl)sulfonylphenol (D-8) and 4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (TGSA) were acquired from Toronto Research Chemicals (Toronto, Canada). The internal standards (IS) Bisphenol A-d_6 diglycidyl Ether (BPA-d_6) and bis(4-hydroxyphenyl) Sulfone-d_8 (BPS-d_8) were also acquired from Toronto Research Chemicals (Toronto, Canada).

Stock solutions of individual bisphenols (2 mg·mL^{-1}) and of IS (BPS-d_8 and BPA-d_6) (5 mg·mL^{-1}) were prepared in MeOH and stored at -20ºC. Intermediate and working solutions were prepared by appropriate dilution in MeOH and also stored at -20ºC.

2.2. Apparatus and sample analysis

Bisphenols were analysed using an Agilent Technologies 1200 LC system with a Phenomenex Luna® C_8 column (2.0 mm i.d., 100 mm length,

3.0 µm particle size) preceded by a Phenomenex KJ 0-4282 Guard column. The LC was coupled to an Agilent Technologies 6420 Triple Quadrupole mass spectrometer equipped with an electrospray ionization (ESI) source operating in negative mode. In order to avoid background contamination of BPA coming from the LC instrument, a LC column Agilent Eclipse Plus C8 5 µm, 4.6 mm x 50 mm was inserted before the injector. The optimal source parameters were: gas temperature, 300°C; gas flow, 11.0 $L \cdot min^{-1}$; nebulizer gas pressure, 15 psi; capillary voltage, -4500 V; MS1 heater, 100°C; MS2 heater, 100°C.

The mobile phase was made up of Milli-Q water (A) and MeOH (B) at a flow rate of 0.25 $mL \cdot min^{-1}$ with a gradient consisting in: initial 100% A hold for 1 min and decreased to 30% in 5 min, holding for 7 min, increased B to 100% and maintained for 6 min and finally re-conditioning for 7 min. *Quantitative analysis MassHunter workstation* software from Agilent Technologies was used for quantification of bisphenols, using the deuterated internal standard BPA-d_6 (except for BPS, for which BPS-d_8 was used). The MRM transitions for target masses are given in Table S1. BPA, BPF, BPS, BPS-MAE, D8 and TGSA were analyzed in ESI negative ionization mode. Raw data were controlled and processed using Agilent MassHunter Software® (version B.07.00).

2.3. Analysis of bisphenols

2.3.1. Sample collection

Samples (n=47) were collected in Spain between 2017 and 2018 from different microenvironments (a microenvironment is a small place with specific features such as temperature, amount of light, moisture content, etc.). The microenvironments were living rooms (n=16), bedrooms (n=16), cars (n=11) and offices (n=4). Results from the analysis of public microenvironments (PME) from our previous study (n=10; two electronic shops, two clothing shops, one sport clothing shop, one decoration shop,

three bazaars and one cafeteria) were taken into account for comparison [14].

Sampling was carried out using vacuum cleaners with a collection device containing disposable nylon filters of 40 μm mesh (Dustream, Indoor Technologies, Cardiff, UK). Dust was collected on the whole floor and at low surfaces (floor plinths, wooden or metallic furniture with a height of maximum ~1 m) of bedrooms, living rooms and offices (size ~9-25 m^2) and on the interiors of cars. The collection device was cleaned with water between microenvironments and a new nylon filter was inserted. All samples were homogenized and sieved to 0.5 mm before analysis. The sieve was thoroughly rinsed with water and then with ethanol between samples.

Table S1. MRM transitions, dwell time, fragmentor voltage and collision energy. Quantifiers for bisphenols are indicated in bold

Compound	Precursor ion (m/z)	Product ion (m/z)	Dwell time (ms)	Fragmentor (V)	Collision energy (eV)
BPA	**227.1**	**212.2**	**50**	**100**	**20**
BPA	227.1	113.0	50	100	24
BPF	**199.0**	**105.0**	**50**	**100**	**25**
BPF	199.0	93.0	50	100	30
BPS	**249.0**	**108.0**	**50**	**100**	**20**
BPS	249.0	92.1	50	100	32
BPS-MAE	**289.1**	**248.1**	**50**	**100**	**20**
BPS-MAE	289.1	184.1	50	100	30
D8	**291.1**	**248.0**	**50**	**100**	**25**
D8	291.1	184.1	50	100	25
TGSA	**329.1**	**132.1**	**50**	**100**	**25**
TGSA	329.1	148.1	50	100	25

2.3.2. Bisphenols extraction

The analytical method, validated in our previous study, was based on the use of supramolecular solvents (SUPRAS) [14]. SUPRAS synthesis and extraction/clean-up was carried out in a single step. Aliquots of 200 μL of hexanol, 200 μL of THF and 800 μL of water and approximately 25 mg of dust sample were added to 2 mL Eppendorf microtubes. Samples were previously spiked with 25 μL of IS (mix of BPA-d_6 and BPS-d_8 at 5 mg·L^{-1}). Mixtures were vortexed during 5 min and centrifuged at 10,000 rpm for 20 min. After that, phase-separation occurred (SUPRAS phase stands at the top, equilibrium solution at the middle and solid sample at the bottom, see Figure S1). A volume of 150 μL of the SUPRAS top layer was collected and transferred to an LC vial with insert. Finally, aliquots of 3 μL were measured by LC-MS/MS.

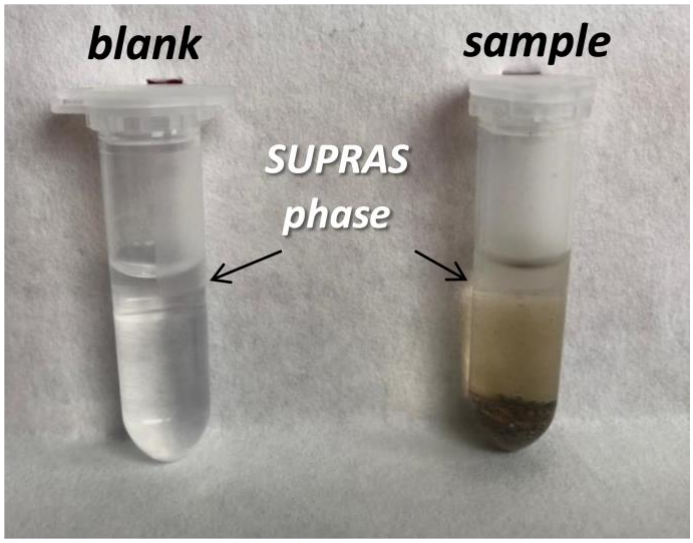


Figure S1. *Left: SUPRAS blank (top layer) and equilibrium phase (bottom layer). Right: SUPRAS (top layer) after extraction, equilibrium phase (in the middle) and sample dust (in the bottom).*

2.3.3. Statistical Analysis

One-way ANOVA and Tukey HSD tests were performed to investigate differences on the levels of each analyte between microenvironments. Correlations between the levels of bisphenols in each microenvironment were studied with Pearson correlation. Results were considered significant with P values less than 0.05. Values below the quantification limit (semi-quantitative values) were considered for the tests while those below the detection limits were not considered.

3. Results and discussion

3.1. Bisphenols concentrations in indoor dust

Table 2 shows concentration range, mean, median and detection frequency for each analyte in each microenvironment. Sample individual concentrations are specified in tables S2-S5.

As expected, BPA was the bisphenol with the highest concentration in all samples and microenvironments due to its widespread use. Values up to 3,803, 4,444, 10,848, 12,696 and 13,846 ng·g^{-1} were found in offices, public microenvironments [14], bedrooms, cars and living rooms, respectively. BPS (282-736 ng·g^{-1}) and BPF (57-659 ng·g^{-1}) followed in maximum concentration levels, which are common BPA replacements. The detection frequency of BPA, BPS and BPF was of 100%, 70-100% and 73-100%, respectively, in the different microenvironments

Regarding the emerging replacements (BPS-MAE, D8 and TGSA), the maximum level of BPS-MAE was 529 ng·g^{-1} and it was found in a bedroom sample. Maximum levels of D8 and TGSA were 128 and 356 ng·g^{-1}, respectively, and were both measured in car samples. Median values of these three compounds were around 2 - 40 times lower than those of BPF and BPS in all the microenvironments. The highest concentrations and

detection frequencies of BPS-MAE, D8 and TGSA were found in cars (above ~50%) with the exception of TGSA frequently found in all the microenvironments (above ~70%). Indeed, values and detection frequencies of these compounds in cars were similar to those reported in shops [14]. Levels in cars were slightly higher than in shop (median values in the range 19 - 58 ng·g^{-1} in cars and 20 - 23 ng·g^{-1} in shops) although the differences between these two microenvironments were not statistically significant P>0.1. Although BPS-MAE, D8 and TGSA have only been reported in thermal paper [7-10, 15], these results suggest that they may be used in products related to car interiors too. Mean concentrations of BPA, BPS, BPF, BPS-MAE, D8 and TGSA in cars were 5,030, 216, 241, 30, 36 and 89 ng·g^{-1}, respectively. Furthermore, they may be used too in other household products which could explain the relatively high levels (>100 ng·g^{-1}) of BPS-MAE, TGSA and D8 found in dust from two bedrooms and two living rooms.

Table 2. Levels of target compounds and IS recoveries in indoor dust from different microenvironments

		Analytes (concentration ng/g)						IS (recovery, %)	
		BPA	BPF	BPS	BPS-MAE	D8	TGSA	BPA-IS d_8	BPS-IS
Public microenvironments (n=10) [14]	Range	192 - 4,444	Detected - 183	n.d. - 736	n.d. - 79	n.d. - 58	n.d. - 48	71-108	69-95
	Mean[a]	1,883	79	290	20	23	22	89	87
	Median[a]	1,739	60	193	6	20	22	85	91
	Detection percentage (%)	100	100	70	50	70	90		
Bedrooms (n=16)	Range	140 - 10,848	n.d. - 120	n.d. - 711	n.d. - 529	n.d. - 79	n.d. - 34	61-100	66-105
	Mean[a]	1,817	59	173	-	32	12	80	88
	Median[a]	1,001	48	135	-	11	9	80	87
	Detection percentage (%)	100	94	88	13	25	69		
Living rooms (n=16)	Range	n.d. - 13,846	n.d. – 180	n.d. – 483	n.d.- 187	n.d. - <LOQ	n.d. – 282	62-111	62-113
	Mean[a]	2,533	78	199	-	-	41	85	86
	Median[a]	1,010	68	192	-	-	5	85	85
	Detection percentage (%)	94	75	81	6	6	69		
Cars (n=11)	Range	Detected- 12,696	n.d. – 659	59 – 439	n.d. - 67	n.d. - 128	n.d. - 356	81-110	64-101
	Mean[a]	5,030	241	216	30	36	89	94	79
	Median[a]	3,353	122	205	33	19	58	92	79
	Detection percentage (%)	100	73	100	55	55	82		
Offices (n=4)	Range	1,329 - 3,803	n.d. - 57	214 - 282	-	n.d. - 8	n.d. -10	94-105	91-98
	Mean[a]	2,077	57	243	-	-	7	100	94
	Median[a]	1,589	57	239	-	-	7	102	94
	Detection percentage (%)	100	75	100	0	25	75		

[a]Values were only calculated when we found three or more positive samples

Table S2. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different bedrooms and recoveries of internal standards

	Concentrations						Recoveries	
	BPA	BPF	BPS	BPS-MAE	D-8	TGSA	BPA-d_6	BPS-d_8
Bedroom 1	5,930	<LOQ	295	n.d.	8	18	78	90
Bedroom 2	1,587	63	217	n.d.	<LOQ	6	84	85
Bedroom 3	10,848	106	194	n.d.	11	19	65	83
Bedroom 4	1,048	47	64	121	n.d.	4	100	99
Bedroom 5	953	21	128	n.d.	n.d.	<LOQ	89	91
Bedroom 6	1,213	<LOQ	130	n.d.	n.d.	n.d.	90	105
Bedroom 7	1,389	49	215	n.d.	n.d.	9	83	88
Bedroom 8	721	<LOQ	39	529	79	34	95	105
Bedroom 9	417	120	n.d.	n.d.	n.d.	9	74	95
Bedroom 10	697	<LOQ	n.d.	n.d.	n.d.	n.d.	61	85
Bedroom 11	1,311	<LOQ	711	n.d.	n.d.	n.d.	71	83
Bedroom 12	322	n.d.	141	n.d.	n.d.	n.d.	87	82
Bedroom 13	140	<LOQ	26	n.d.	n.d.	n.d.	89	66
Bedroom 14	196	<LOQ	140	n.d.	n.d.	6	65	80
Bedroom 15	403	38	107	n.d.	n.d.	5	87	84
Bedroom 16	1,891	25	15	n.d.	n.d.	9	82	77

n.d.: non-detected

Table S3. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different living rooms and recoveries of internal standards

	Concentrations						Recoveries	
	BPA	BPF	BPS	BPS-MAE	D-8	TGSA	BPA-d_6	BPS-d_8
Living room 1	2,461	87	309	n.d.	n.d.	<LOQ	95	97
Living room 2	2,629	<LOQ	219	n.d.	n.d.	3	92	56
Living room 3	1,325	76	131	n.d.	n.d.	3	87	87
Living room 4	978	33	68	n.d.	n.d.	<LOQ	85	87
Living room 5	782	62	148	n.d.	n.d.	n.d.	105	105
Living room 6	1,116	58	141	n.d.	n.d.	<LOQ	83	101
Living room 7	13,846	<LOQ	87	n.d.	n.d.	2	80	81
Living room 8	2,325	50	234	187	<LOQ	n.d.	111	113
Living room 9	418	180	238	n.d.	n.d.	7	69	84
Living room 10	9,604	n.d.	192	n.d.	n.d.	n.d.	86	65
Living room 11	88	<LOQ	n.d.	n.d.	n.d.	n.d.	85	90
Living room 12	n.d.	n.d.	n.d.	n.d.	n.d.	4	82	86
Living room 13	352	n.d.	n.d.	n.d.	n.d.	n.d.	81	62
Living room 14	245	<LOQ	2	n.d.	n.d.	9	71	77
Living room 15	813	74	483	n.d.	n.d.	18	62	77
Living room 16	1,010	n.d.	335	n.d.	n.d.	282	86	85

n.d.: non-detected

Table S4. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different cars and recoveries of internal standards

	Concentrations						Recoveries	
	BPA	BPF	BPS	BPS-MAE	D-8	TGSA	BPA-d_6	BPS-d_8
Car 1	3,947	<LOQ	357	n.d.	n.d.	n.d.	88	65
Car 2	5,501	101	439	43	19	n.d.	82	70
Car 3	2,511	659	179	2	22	151	89	82
Car 4	1,261	n.d.	218	n.d.	n.d.	120	88	67
Car 5	12,697	<LOQ	223	67	128	356	84	79
Car 6	1,403	142	59	34	n.d.	7	81	93
Car 7	1,178	<LOQ	241	n.d.	n.d.	6	92	64
Car 8	<LOQ	n.d.	96	33	3	58	83	95
Car 9	15,096	n.d.	205	n.d.	<LOQ	17	86	75
Car 10	3,925	<LOQ	180	3	5	8	81	79
Car 11	2,782	63	177	n.d.	n.d.	76	110	101

n.d.: non-detected

Table S5. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different offices and recoveries of internal standards

	Concentrations						Recoveries	
	BPA	BPF	BPS	BPS-MAE	D-8	TGSA	BPA-d_6	BPS-d_8
Office 1	3,803	n.d.	214	n.d.	8	n.d.	87	88
Office 2	1,382	<LOQ	246	n.d.	n.d.	3	105	94
Office 3	1,796	<LOQ	232	n.d.	n.d.	10	102	98
Office 4	1,329	57	282	n.d.	n.d.	<LOQ	94	92

n.d.: non-detected

3.2. Correlations between target compounds and differences between microenvironments

Correlation values between analytes in each microenvironment and in all the samples were investigated (see Table S6). Correlations were performed when analytes were found in at least 4 samples. Taking into account all the positive samples, a statistically significant positive correlation ($r=0.624$, $p<0.01$, $n=16$) was observed between D8 and TGSA.

This pair of BPA analogues also showed a statistically significant positive correlation in bedrooms ($r=0.950$, $p<0.05$, $n=4$). In fact, we also observed a positive correlation between D8 and TGSA in the other microenvironments for which values could be calculated, namely in cars ($r=0.84$, $n=5$) and in shops ($r=0.64$, $n=7$), but they were not statistically significant although their p values were low ($p=0.12$ and $p=0.08$, respectively). We also observed statistically significant positive correlations between BPA and D-8 ($r=0.87$, $p<0.01$, $n=7$), and BPA and TGSA ($r=0.81$, $p<0.01$, $n=8$) in public microenvironments. However, these mixtures have not been frequently observed in thermal paper studies [7-10].

BPF also showed a statistically significant positive correlation with D8 ($r=0.83$, $p<0.05$ $n=7$) in public microenvironments. However, BPF has not been reported in thermal paper [7-10,16]), so its use in other type of products could explain this correlation.

Finally, BPA and BPS were also significantly correlated when all the samples were considered, although with a low value ($r=0.39$, $p<0.01$, $n=49$). This correlation may be due to the fact that certain microenvironments were exposed to higher number of consumer products easily containing bisphenols and that BPA and BPS are the most widely used.

We investigated differences between microenvironments for each analyte by one-way ANOVA and Tukey HSD tests. We only found statistically significant differences between offices and cars for BPF and TGSA and between bedrooms and cars for TGSA. Mean concentrations of BPF and TGSA in cars were about 5 and 13 times higher than in offices, respectively, and with similar detection percentages. The mean concentration of TGSA in cars was also higher than mean value in bedrooms (about 7 times higher) with similar detection percentages too.

Table S6. Pearson correlation values and their respective p-values for each couple of bisphenols in all microenvironments. Highlighted values are statistically significant (p<0.05) and show positive correlations (r>0.6).

	All samples n=57	p value	Living room n=16	p value	Bedroom n=16	p value	PME n=10	p value	Office n=4	p value	Cars n=11	p value
BPA-BPF	-0.001	0.9	-0.4	0.2	0.2	0.5	-0.4	0.3	-0.8	0.5	-0.3	0.6
BPA-BPS	0.4	0.006	0.3	0.2	0.3	0.2	0.08	0.9	-0.8	0.2	0.4	0.2
BPA-BPSMAE	-0.06	0.9	-	-	-	-	0.7	0.2	-	-	0.2	0.7
BPA-D8	0.08	0.7	-	-	-0.3	0.7	**0.9**	**0.01**	-	-	0.2	0.7
BPA-TGSA	0.3	0.09	-0.3	0.4	0.4	0.3	**0.8**	**0.01**	-	-	0.2	0.5
BPS-BPF	0.2	0.1	0.5	0.1	0.3	0.3	0.5	0.3	-	-	-0.3	0.4
BPS-BPSMAE	-0.5	0.07	-	-	-	-	-0.6	0.4	-	-	-0.01	0.9
BPS-D8	-0.06	0.8	-	-	-0.8	0.2	0.4	0.4	-	-	0.4	0.4
BPS-TGSA	0.1	0.5	0.1	0.8	-0.09	0.8	-0.4	0.4	-	-	0.3	0.4
BPF-BPSMAE	-0.5	0.08	-	-	-	-	-0.07	0.9	-	-	-0.6	0.3
BPF-D8	-0.06	0.8	-	-	-0.7	0.3	**0.8**	**0.02**	-	-	-0.2	0.8
BPF-TGSA	0.2	0.3	0.2	0.7	0.1	0.7	-0.3	0.5	-	-	0.2	0.7
BPSMAE-D8	0.05	0.9	-	-	-	-	0.2	0.8	-	-	0.4	0.5
BPSMAE-TGSA	0.05	0.9	-	-	-	-	0.3	0.6	-	-	0.2	0.7
D8-TGSA	**0.6**	**0.001**	-	-	**0.9**	**0.05**	0.6	0.1	-	-	0.8	0.08

Correlations were performed when analytes were found in at least 4 samples.

3.3. Human exposure to bisphenols via indoor dust ingestion

Human exposure via dust ingestion was estimated using the method described by Abdallah and Covaci [17]. Two different scenarios of exposure were considered, namely average and worst-case, which were calculated with the mean, median and maximum concentrations in all the microenvironments (houses as living rooms and bedrooms, offices, cars and public microenvironments). The time spent in each of microenvironment according to the age (adults and toddlers) was also taken into account. The equation to estimate the exposure was as follow [17]:

$$\sum_{(evdi)} = [(C_H F_H) + (C_O F_O) + (C_C F_C) + (C_{PME} F_{PME})] \cdot RR$$

where $\sum_{(evdi)}$ is the total daily human exposure via dust ingestion (ng·day^{-1}); C is the concentration (ng·g^{-1}) of homes (C_H), offices (C_o), cars (C_c) and public microenvironments (C_{PME}); F is the fraction (%) of time spent in each microenvironment: 63.8% and 86.1% in homes (F_H), 22.3% and 0% in offices (F_o), 4.1% and 4.1% in cars (F_c) and 5.1% and 5.1% in public microenvironments (F_{PME}), for adults and toddlers, respectively [18]; and RR is the daily dust ingestion rate (mg·day^{-1}) [17]. In the average case, RR

was 20 mg·day^{-1} for adults and 40 mg·day^{-1} for toddlers, and in the worst case, RR was 60 mg·day^{-1} for adults and 100 mg·day^{-1} for toddlers [19].

Table 3 shows the estimated exposure via dust ingestion (ng·day^{-1}). Maximum exposure levels were 14, 2 and 7 ng·day^{-1} in adults and 32, 4 and 15 ng·day^{-1} in toddlers for BPS-MAE, D8 and TGSA, respectively. These values were lower but in the same order of magnitude than those of BPS (30 ng·day^{-1} in adults and 57 ng·day^{-1} in toddlers) and BPF (9 ng·day^{-1} in adults and 17 ng·day^{-1} in toddlers). Mean exposure values of BPS-MAE, D8 and TGSA were about 6-100 times lower than those estimated for BPS and BPF. The lower values measured for BPS-MAE, D8 and TGSA and lower detection frequencies in houses are in agreement with their expected lower market volume in comparison with BPA (and BPS and BPF).

Table 3. Estimated exposure of bisphenols via dust ingestion (ng·day^{-1}) in adults and toddlers

		Adults		Toddlers	
		Average	High	Average	High
Mean	BPA	42.9	128.7	86.6	216.4
	BPF	1.4	4.2	2.9	7.3
	BPS	3.9	11.8	7.3	18.3
	BPS-MAE	<0.1	0.1	<0.1	0.2
	D8	<0.1	0.2	0.1	0.3
	TGSA	0.4	1.3	1.1	2.6
Median	BPA	24.5	73.5	43.8	109.6
	BPF	1.9	3.6	2.4	5.9
	BPS	3.2	9.7	5.6	13.9
	BPS-MAE	<0.1	0.1	<0.1	0.2
	D8	<0.1	0.1	<0.1	0.2
	TGSA	0.2	0.6	0.4	1.0
Maximum	BPA	189.5	568.3	455.1	1137.8
	BPF	2.9	8.7	6.6	16.6
	BPS	10.0	30.0	22.8	57.1
	BPS-MAE	4.7	14.1	12.6	31.5
	D8	0.7	2.1	1.7	4.2
	TGSA	2.4	7.2	6.1	15.3

Table S7 shows estimated human exposure values reported by other authors via dust ingestion of BPA, BPS and BPF according to different scenarios and in nine different countries (Sweden, US, China, Japan, Korea, Greece, India, Colombia, Romania) [6,20,21]. Values were determined by the amount of ingested dust per day considered in each study (30 - 100 mg) and by the formula applied for the estimation of the exposure, considering or not indoor exposure fractions (hours spent over a day in an indoor microenvironment). Maximum ingestion levels of BPA, BPS and BPF in our study were in the ranges 190 - 1,138, 10 - 57 and 3 - 17 ng·day^{-1}, respectively. These values were in line with those previously reported for BPA (17.6 - 2,052 ng·day^{-1}) and in the low range for BPS (0.16-798 ng·day^{-1}) and BPF (1.26 - 1,109 ng·day^{-1}). Nevertheless, the highest values reported in these studies came from US, Japan and Korea and not from European countries.

Median ingestion levels (adults) of BPA, BPS and BPF were in the ranges 24-73, 3-10, 2-4 ng·day^{-1}, respectively, in samples from Spain. These values were within the range of those reported in other European countries, namely 19-93 for BPA, 2-51 for BPS and 0.08-47 ng·day^{-1} for BPF in Greece and Romania (see Table S7).

The maximum dust ingestion values for BPA (adults and toddlers) estimated in our study were compared with the RfD (reference dose) of 50 μg·Kg bw^{-1}·day^{-1} set by EPA [22] and the temporary TDI (tolerable daily intake) of 4 μg·Kg bw^{-1}·day^{-1} set by UE [23]. Nevertheless, dust is expected to have a minor contribution to the overall exposure in comparison with food. [13] Body weights of 70 and 12 Kg were taken into account for adults and toddlers, respectively, as recommended by the European Food Safety Authority. [24] Estimated values (worst-case scenario) were by far lower than the established limits and in the range 3-8 ng·Kg bw^{-1}·day^{-1} for adults and 38-95 ng·Kg bw^{-1}·day^{-1} for toddlers.

Table S7. Levels of bisphenols in dust, ingestion and dust ingestion rate and formula used.

Countries	Analytes	Concentration in dust (ng·g^{-1})			Estimated ingestion (ng·day^{-1})[a]			I_{dust} (g·day^{-1})	Estimated daily intake (EDI; ng·day^{-1}·Kg^{-1})[b]	Ref.
		Mean	Median	Maximum	Mean	Median	P95			
Sweden n=100	BPA	1,200	1,300	1,100	35	-	176	0.06	$\frac{C_{dust} * I_{dust}}{BW}$	[20]
					-	-	-			
	BPS	260	240	3,800	7	-	11			
					-	-	-			
	BPF	-	-	4,400	-	-	-			
					-	-	-			
US n=38	BPA	1,700	1,600	-	-	127	544	0.1	$\frac{C_{dust} * I_{dust} * IEF}{BW}$	[6]
					-	70	301	0.05		
	BPS	620	630	-	-	49	798	0.1		
					-	27	445	0.05		
	BPF	22	49	-	-	4	16	0.1		
					-	2	9	0.05		
China n=55	BPA	360	630	-	-	50	281	0.1	$\frac{C_{dust} * I_{dust} * IEF}{BW}$	[6]
					-	28	157	0.05		
	BPS	130	170	-	-	13	138	0.1		
					-	8	77	0.05		
	BPF	21	38	-	-	3	44	0.1		
					-	2	25	0.05		
Japan n=22	BPA	2,830	2,700	-	-	213	969	0.1	$\frac{C_{dust} * I_{dust} * IEF}{BW}$	[6]
					-	118	539	0.05		
	BPS	820	810	-	-	64	161	0.1		
					-	36	89	0.05		
	BPF	45	57	-	-	5	66	0.1		
					-	3	37	0.05		
Korea n=41	BPA	4,070	3,260	-	-	257	2.052	0.1	$\frac{C_{dust} * I_{dust} * IEF}{BW}$	[6]
					-	144	1.140	0.05		
	BPS	430	360	-	-	29	106	0.1		
					-	16	59	0.05		
	BPF	500	450	-	-	35	1.109	0.1		
					-	20	618	0.05		
Greece n=28	BPA	1,700	1,500	-	-	93	122	0.06	$\frac{C_{dust} * I_{dust}}{BW}$	[21]
					-	50	65	0.03		
	BPS	1,500	860	-	-	51	165	0.06		
					-	27	88	0.03		
	BPF	5,500	780	-	-	47	750	0.06		
					-	25	400	0.03		
India n=35	BPA	360	130	-	-	8	44	0.06	$\frac{C_{dust} * I_{dust}}{BW}$	[21]
					-	4	21	0.03		
	BPS	12	4.2	-	-	0.2	1	0.06		
					-	0.1	0.6	0.03		
	BPF	29	6.7	-	-	0.4	3	0.06		
					-	0.3	1	0.03		
Colombia n=42	BPA	420	120	-	-	7	33	0.06	$\frac{C_{dust} * I_{dust}}{BW}$	[21]
					-	4	18	0.03		
	BPS	3.7	2.4	-	-	0.2	0.3	0.06		
					-	0.08	0.2	0.03		
	BPF	69	33	-	-	2	6	0.06		
					-	0.8	3	0.03		
Romania n=23	BPA	680	600	-	-	36	48	0.06	$\frac{C_{dust} * I_{dust}}{BW}$	[21]
					-	19	26	0.03		
	BPS	380	82	-	-	5	39	0.06		
					-	2	21	0.03		
	BPF	41	2.0	-	-	0.2	4	0.06		
					-	0.08	2	0.03		

Values for worst-case (top) and average (bottom) scenarios are given; Estimated ingestion values were calculated from reported EDI. I_{dust}: Dust ingestion rate (g·day^{-1}); C_{dust}: concentration in dust (ng·g^{-1}); BW: body weight (Kg); IEF: indoor exposure fraction.

4. Conclusions

Median values of BPS-MAE, D-8 and TGSA were around 2-40 times lower than those of BPF and BPS in dust from all the microenvironments collected in Spain. The highest detection frequency and levels were found in cars (median values 19 - 58 ng·g^{-1}). The estimated exposure via dust

ingestion of BPS-MAE, D-8 and TGSA was also low in comparison with other bisphenols and only comparable to BPF and BPS in the worst-case scenario (2 - 14 and 4 - 32 ng·day^{-1} for adults and toddlers, respectively). However, these values could increase in the future as a consequence of the legislative restrictions on the use of BPA.

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Supramolecular solvent-based microextraction of aryl-phosphate flame retardants in indoor dust from houses and education buildings in Spain

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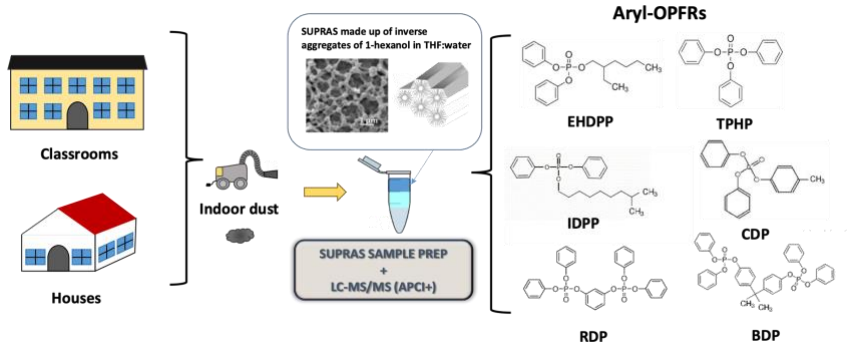

Highlights

- SUPRAS treatment was validated for determination of aryl-OPFRs in indoor dust.
- TPHP was the most abundant OPFR in houses and EHDPP and IDPP in education buildings.
- Median levels of ∑aryl-PFRs were 2 times higher in classrooms compared to houses.
- Exposure was the same for toddlers staying at home than those going to kindergarten.
- University exposure levels were higher than in other education centers.

Abstract

Aryl-phosphate flame retardants (aryl-OPFRs) are flame retardants or plasticizers (among other functions) that can be found in a wide variety of products, from furniture and textiles to cars and electronic equipment. There is an increasing concern about the human exposure to these contaminants due to their ubiquity (as additives they can be easily released from the product to the environment) and potential toxicity. In this study, we investigated the presence of six representative aryl-OPFRs, two well-known aryl-OPFRs (triphenyl phosphate, TPHP and 2-ethylhexyl diphenyl phosphate, EHDPP), two novel aryl-OPFRs (cresyl diphenyl phosphate, CDP and isodecyl diphenyl phosphate, IDPP) and two oligomeric aryl-OPFRs [bisphenol A bis(diphenyl phosphate), BDP and resorcinol bis(diphenyl phosphate, RDP], in indoor dust from houses and education buildings from Spain. Sample treatment was carried out by a novel and simple procedure based on supramolecular solvents (SUPRAS) prior to LC-MS/MS analysis. The median Σaryl-OPFRs was two times higher in classrooms than in houses, being particularly high at University classrooms. The most abundant aryl-OPFR in houses was TPHP (median 497 ng $\cdot g^{-1}$) while EHDPP (median 407 ng $\cdot g^{-1}$) and IDPP (median 403 ng $\cdot g^{-1}$) were dominant in classrooms. This is the first study reporting IDPP, BDP and RDP in different education buildings.

Keywords: *supramolecular solvents, aryl-phosphate flame retardants, indoor dust, ingestion.*

1. Introduction

Flame retardants (FRs) are widely used in products, e.g. electric equipment, furniture, textiles or vehicles, among others, to prevent ignition and make them more resistant to fire (Alaee et al. 2003). Restrictions on the use of legacy FRs (mainly polybrominated diphenyl ethers, PBDEs) due to their toxicity, persistence and bioaccumulation, have led to an increase in the use of alternatives, such as organophosphate flame retardants (OPFRs) (US EPA, 2016, Yang et al. 2019). The global consumption of FRs reached a volume of 2.5 million tonnes in 2015 (Global flame retardant market report, 2017) of which 20% is estimated to be OPFRs (EFRA, 2007). OPFRs are also used as plasticizers, anti-foaming agents, extreme pressure additives and anti-wear agents (Wei et al. 2015). They are not bound to materials and can therefore easily migrate into the environment by volatilization, abrasion or dissolution (Salthammer et al. 2003, Marklund et al. 2005). As a consequence, OPFRs have been detected in indoor dust, air, water, soil, sediment and biota (Wei et al. 2015). Human exposure to these ubiquitous contaminants occurs via different pathways. So, we can be exposed through skin contact (dermal absorption) with products or dust, by the inhalation or ingestion of dust particles and by ingestion of contaminated food. Although the toxic properties of OPFRs have been studied in a lesser extent than those of PBDEs, findings have shown evidence of neurotoxicity, developmental toxicity, damage to the reproductive function, endocrine disruption, and carcinogenicity (Wei et al. 2015, Yang et al. 2019).

Indoor dust has become a relevant matrix for the indoor exposure assessment to organic contaminants, especially for those coming from indoor materials and products (Hou et al. 2016). The presence of OPFRs in indoor dust has been reported worldwide at ng/g to mg/g levels and with high detection frequencies (Wei et al. 2015, Ali et al. 2017). OPFRs are usually classified in three groups based on their composition: alkyl-OPFRs, aryl-OPFRs and chlorinated OPFRs (Hou et al. 2016). A recent study of Li et al. (2019) reported levels of 20 OPFRs in 341 dust samples

from houses located in 12 countries. Levels of ΣOPFRs ranged from 49.4 to 249,000 ng/g with median concentrations of 270 ng/g of aryl-OPFRs and 21.9 ng/g of oligomeric OPFRs. In this study we analyze a representative group of aryl-OPFRs, namely bisphenol A bis(diphenyl phosphate) (BDP), cresyl diphenyl phosphate (CDP), 2-ethylhexyl diphenyl phosphate (EHDPP), isodecyl diphenyl phosphate (IDPP), resorcinol bis(diphenyl phosphate) (RDP) and triphenyl phosphate (TPHP). While EHDPP and TPHP have been widely reported, data about novel aryl-PFRs, such as IDPP and CDP and about oligomeric OPFRs, such as BDP and RDP is more limited (Brandsma et al. 2013, Kademoglou et al. 2017, Li et al. 2019). To the best of our knowledge, the presence of these novel (IDPP and CDP) and oligomeric aryl-OPFRs (BPD and RDP) in indoor dust from education buildings, has not been investigated before. Furthermore, these compounds have not been determined in house dust from Spain yet.

Some studies and technical reports have documented moderate to high toxicity, persistence and/or bioaccumulation potential for the selected OPFRs. The study of Du et al. (2015) showed that aryl-OPFRs had greater cardiac developmental toxicity than alkyl-OPFRs and that CDP showed the greatest toxicity. RDP and BDP have been reported to be more persistent than other OPFRs due to their high hydrophobicity and low water solubility and showed in vivo (eco)toxicity that varied from low to high, with special concern for the TPHP impurities present in the commercial products (Waaijers et al., 2012). Table S1 summarize the main toxic and environmental hazardous properties reported by technical documents from the UK and the Danish Environmental Agencies.

In this study, we analyzed aryl-OPFRs in dust samples using supramolecular solvents (SUPRAS). SUPRAS are nanostructured liquids produced by spontaneous self-assembly and coacervation of a colloidal dispersion of amphiphilic aggregates by the presence of a coacervation-inducing agent (pH or temperature change, poor solvent for the amphiphile and/or addition of salt) (Ballesteros-Gómez et al. 2019). They act as multimode extractants that offer a variety of binding interactions

(ionic, anionic, hydrogen bonds, dispersion interaction, etc.), which depend on the functional groups of the amphiphile/s and the nature of the coacervation-inducing agent. They also offer microenvironments of different polarity and feature restricted access properties due to their internal structure (Ballesteros-Gómez & Rubio, 2012; Ballesteros-Gómez et al. 2019; Caballo et al. 2017). The generic sample treatment of dust (a complex and heterogeneous matrix) benefits from these properties. The use of SUPRAS for extraction of contaminants in indoor dust has been recently reported by our research group for the analysis of bisphenols (Dueñas-Mas et al. 2019a). The simplicity of the proposed SUPRAS method (it consists in a simple single step of extraction/clean-up based on stirring and centrifugation) offers advantages over reported studies for the determination of OPFRs in dust (e.g. Kademoglou et al. 2017; Velázquez-Gómez et al., 2019; Li et al., 2019; De la Torre et al., 2020; Percy et al., 2020). These strategies are mainly based on multiple steps of solvent extraction (methanol, hexane:acetone or dichloromethane) and clean-up, which is mainly based on solid-phase extraction (Oasis HLB, Florisil, aminopropyl silica catridges, etc.). These methods involve a high consumption of organic solvents and materials (at the extraction or clean-up steps) with several evaporation and reconstitution steps, being expensive, not environmentally friendly, tedious and long and they are also prone to blank contamination, which is particularly relevant for ubiquitous contaminants as OPFRs.

The objective of the present study was to develop a simple method for the analysis of aryl-OPFRs in indoor dust and to investigate the presence of these compounds in houses and education buildings from South Spain. Differences between these two microenvironments and correlations between the levels of the target compounds were investigated. Finally, we estimated the human exposure via dust ingestion in South Spain, discerning between toddlers and adults and according to different possible scenarios of exposure.

Table S1. General hazard parameters (human health and the environment) for the target compounds

	Lowest NOEC (mg/L)[a]	BCF (L/Kg)[a]	PBT criteria[a]	Hazard Classification[a]	GreenScreen profile[b]
TPHP	0.032	420	-	N R50/53	M (carcinogenicity); H (endocrine activity); H (systemic toxicity, r); VH (acute and chronic aquatic toxicity)
EHDPP	0.018	934	-	N R50/53	Not reported
CDP	0.014	200	T? (a proposed classification as reprotoxin would trigger the T criterion)	R60 (effects on fertility) N R50/53	H (reproductive toxicity); M (developmental toxicity); M (acute mammalian toxicity); H (systemic toxicity); M (neurotoxicity); M (skin sensitization); VH (acute aquatic toxicity); H (chronic aquatic toxicity); M (persistence); H (bioaccumulation)
IDPP	0.004	330	P and vP, T	N R50/53	Not reported
RDP	0.014	969	P and vP	N R50/53	M (carcinogenicity); M (developmental toxicity); H (endocrine activity); M (systemic toxicity); M (neurotoxicity); VH (acute and chronic aquatic toxicity); M (persistence); H (bioaccumulation)
BDP	Not reported	Not reported	Not reported	Not reported	M (carcinogenicity); H (persistence); M (bioaccumulation)

[a]Data based on the Environmental risk evaluation reports for aryl phosphate esters of the Environment Agency UK (http://publications.environmentagency.gov.uk).

- Abbreviations: NOEC (no observed effect concentration); BFC (biological concentration factor); P (persistent); B (bioaccumulative), T (toxic).
- PBT criteria. P: half-life above 60 days in marine water or above 40 days in freshwater or half-life above 180 days in marine sediment or above 120 days in freshwater sediment. B: BFC>2000. T: NOEC <0.01. vPvB criteria. P: Half-life above 60 days in marine water or freshwater or above 180 days in marine or freshwater sediment. B: BCF> 5000. T: not applicable
- Hazard classification for the environment. N: Dangerous for the environment. R50/53: Very toxic to aquatic organisms

[b]Data based on: Lassen, C; Warmin, M; Brinch, A; Zwicky Burkal; Kjølholt, J; Hagen Mikkelsen, S. 2016. Environmental and health screening profiles of phosphorous flame retardants. The Danish Environmental Protection Agency. (https://www2.mst.dk/Udgiv/publications/2016/01/978-87-93435-23-0.pdf).

- Abbreviations: M (moderate); H (high); VH (very high). See referenced document for toxicity criteria.

2. Experimental section

2.1. Chemicals and reagents

Tetrahydrofuran (THF) and methanol (MeOH) were supplied by VWR – Prolabo Chemicals (Bois, France) and 1- hexanol was obtained from Merck (Darmstadt, Germany). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain). All solvents were of analytical reagent-grade and they were used as supplied.

All aryl-OPFRs were obtained from AccuStandard (New Haven, CT) as 1 mL ampoules (~100 μg/mL of analyte certified concentration in toluene), except TPHP and the internal standard (IS) TPHP-d_{15}, which were acquired as solids from Sigma Aldrich (Zwijndrecht, the Netherlands). The target compounds were bisphenol A bis(diphenyl phosphate) (BDP, CAS 5945-33-5), cresyl diphenyl phosphate (CDP, CAS 26444-49-5), 2-ethylhexyl diphenyl phosphate (EHDPP, CAS 1241-94-7), isodecyl diphenyl phosphate (IDPP, CAS 29761-21-5), resorcinol bis(diphenyl phosphate) (RDP, CAS 57583-54-7) and triphenyl phosphate (TPHP, CAS 115-86-6).

A spike solution of IS (TPHP-d_{15}) was prepared in MeOH at a concentration of 1.25 mg·L^{-1} for both optimization and sample analysis. Stock and working solutions of OPFRs were prepared by dilution in MeOH. All solutions were stored at -20ºC.

2.2. Apparatus and sample analysis

An Agilent Technologies 1200 LC system with a RESTEK C_{18} column (3.0 mm i.d., 100 mm length, 3.0 μm particle size) preceded by a precolumn Phenomenex KJ 0-4282 SecurityGuard Cartridge Kit, Ea, was used for separation of target compounds. The LC system was coupled to an Agilent Technologies 6420 Triple Quadrupole mass spectrometer,

equipped with an APCI source operating in positive mode. Source parameters were as follows: gas temperature, 325°C; gas flow, 4.0 L·min^{-1}; vaporizer, 400 °C; nebulizer gas pressure, 20 psi; capillary voltage, 4500 V; corona current 4 μA.

The chromatographic method and MRM transitions were based in our previous study (Björnsdotter et al., 2017, see Table S2) with modifications.

Table S2. MRM transitions, fragmentor voltage and collision energy. Quantifiers for the target compounds are indicated in bold. The dwell time was 150 ms.

Compound	Precursor ion (m/z)	Product ion (m/z)	Fragmentor (V)	Collision energy (eV)
BDP	**693.2**	**367.2**	**156**	**47**
BDP	693.2	115.2	156	101
CDP	**341.1**	**65.2**	**116**	**89**
CDP	341.1	91.2	116	53
EHDPP	**363.1**	**251.1**	**71**	**11**
EHDPP	363.1	77.1	71	93
IDPP	**391.2**	**251.1**	**81**	**15**
IDPP	391.2	77.1	81	73
RDP	**575.1**	**77.2**	**151**	**115**
RDP	575.1	152.2	151	79
TPHP	**327.1**	**77.1**	**150**	**40**
TPHP	327.1	215	135	30
TPHP-d15	**342.2**	**82.2**	**150**	**135**
TPHP-d15	342.2	222.1	150	135

The mobile phase consisted of Milli-Q water (A) and MeOH (B) at a flow rate of 0.25 mL·min^{-1}. The mobile phase gradient was initial 50% of A during 0.1 min, decreasing to 10% A at 5 min, decreasing to 1% A at 10 min, kept constant at 1% A for 10 min and finally, re-condition for 7 min. Flame retardants were quantified with *Quantitative analysis MassHunter workstation* software from Agilent Technologies. Raw data were controlled and processed using the Agilent MassHunter Software® (version B.07.00).

A vortex-shaker REAX Top (Heidolph, Schwabach, Germany) and a 12 x 1.5 – 2 mL angle rotor Minicen centrifuge from Ortoalresa (Madrid, Spain) were used for sample preparation.

2.3. SUPRAS extraction method validation.

SUPRAS extraction of aryl-OPFRs was validated using a house dust sample containing very low levels of the target compounds (see Table 1 in 3.1.). Fortified samples (and calibration standards) were prepared by spiking them before extraction with a mix of target compounds and a solution of IS. Linearity (10 - 1300 ng·g^{-1}, SUPRAS-based calibration, IS 500 ng·g^{-1}), accuracy (expressed as recovery at three levels 50, 360 and 1,300 ng·g^{-1}, sample size 50 mg), sensitivity (method detection limits, LODs and quantification limits, LOQs) and precision (as intra-day repeatability, expressed as relative standard deviation).

2.3.1. Sample collection

Samples were collected in Córdoba province in Spain during Spring 2019 from classrooms of education buildings (n= 16, including 5 kindergartens, 3 primary schools, 2 high schools and 6 University classrooms located in Rabanales Campus) and houses (living rooms and bedrooms, n= 22). Sampling was carried out using vacuum cleaners with a collection device containing disposable nylon filters of 40 μm mesh (Dustream, Indoor Technologies, Cardiff, UK). Dust was collected on the floor of bedrooms and living rooms and on the floor of classrooms. The collection device was cleaned with water between samples and a new nylon filter was inserted. All samples were homogenized and sieved to 0.5 mm before analysis. The sieve was thoroughly rinsed with water and ethanol between samples.

In order to investigate possible sources of contamination in classes, we sampled plastics and painted walls and doors at a representative University classroom (sample C11, Table S6) with a cutter. The cutter was cleaned with methanol between samples to avoid cross-contamination. Samples were taken from electric appliances, laminate floor and plastics fittings at the floor, walls and doors.

2.3.2. Sample extraction and analysis

Approximately 50 mg of dust sample was weighed in a 2 mL Eppendorf microtube. The IS (20 μL of TPHP-d_{15} at 1.25 mg·L^{-1}) was added to the solid. Finally, we added the SUPRAS components (200 μL of 1-hexanol, 200 μL of THF and 800 μL of Milli-Q water). The SUPRAS was *in situ* and spontaneously produced, and the mixture was vortexed during 5 min for extraction of OPFRs. Then it was centrifuged at 10,000 rpm for 20 min. Around 150 μL of SUPRAS (top layer) were collected and transferred to an LC vial and aliquots of 5 μL were analyzed by LC-MS/MS(APCI+).

Materials from a representative University classroom (around 20 mg aliquots) were extracted with 1 mL of methanol by vortex (1 min) and then left stand for 1 hour to enhance the leaching of aryl-OPFRs. Aliquots of 5 μL were analyzed by LC-MS/MS(APCI+).

2.3.3. Statistical Analysis

The correlation between analytes in each microenvironment was investigated by Spearman correlation (data was not normally distributed, calculated with Shapiro-Wilks tests). Mann-Whitney U tests were performed in order to investigate if concentrations of target compounds were significantly different between microenvironments. Results with p values less than 0.05 were considered significant. For statistical purposes,

levels below limit of quantification (LOQ) were replaced with their semi-quantitative value, while levels below limit of detection (LOD) were replaced by $\frac{\sqrt{2}}{2*LOD}$ (Antweiler et al. 2015).

3. Results and discussion

We employed SUPRAS made up of 1-hexanol (amphiphile) in mixtures of THF and water based on our previous good results with the determination of bisphenols in indoor dust (Dueñas-Mas et al. 2019b). The SUPRAS was generated by simple mixing and centrifuging a mixture of 1-hexanol, THF and water in the presence of the dust sample, so that extraction and SUPRAS formation took place in a single step. Water was the so-called coacervation or self-assembly agent (poor solvent for the amphiphile 1-hexanol). After phase separation, the solid matrix remained at the bottom, an aqueous equilibrium solution stayed at the middle (containing a residual amount of 1-hexanol at a low critical micellar concentration) and the SUPRAS phase (containing most of the amphiphile) was at the top. The internal structure of these SUPRAS has been described as an inverse hexagonal phase with the alcohol groups surrounding the internal aqueous pores and the alkyl chains dispersed in THF as inner layers (Ballesteros-Gómez et al. 2012, Salatti-Dorado et al. 2017). Figure S1 depicts the formation and inner structure of 1-hexanol based SUPRAS. Under the selected synthetic conditions, the average SUPRAS volume per sample was 370 μL (Salatti et al. 2017).

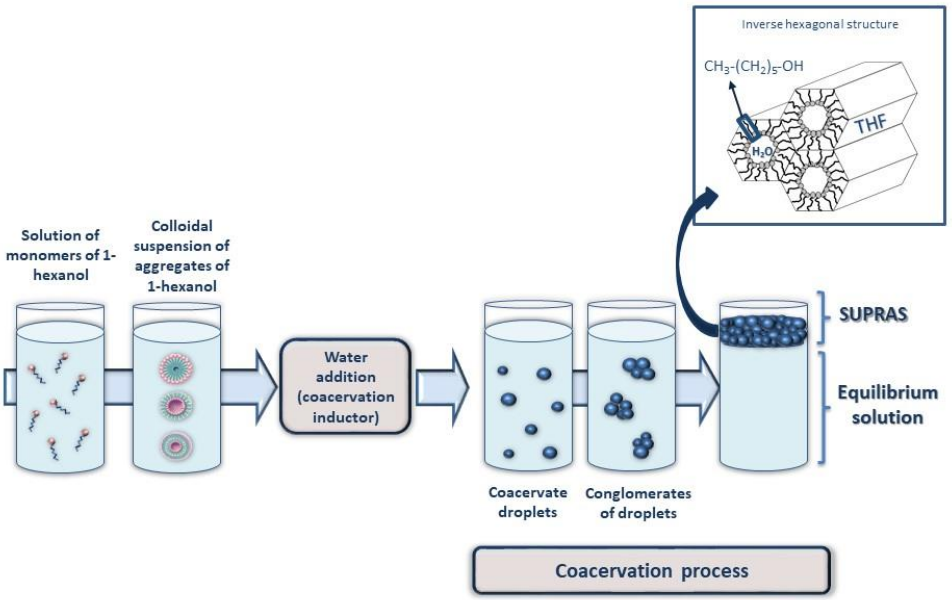

Figure S1. *Scheme of formation and inner structure of 1-hexanol-based SUPRAS.*

As mentioned in the Introduction, the SUPRAS method was advantageous over other reported strategies in terms of simplicity (single-step treatment without evaporation/reconstitution steps), rapidity and low consumption of reagents. Table S3 compares the reported analytical methods for the determination of OPFRs in indoor dust with the present study (sample size, extraction and cleanup-steps and concentration factors).

3.1. Analytical performance and validation

Calibration curves were prepared in SUPRAS (following the same procedure as described in section 2.3.2 but without dust). SUPRAS-based calibration was performed instead of conventional solvent-based calibration to ensure the same injection medium in standards and in samples, since this can slightly influence retention times and ionization. Losses of compounds in the equilibrium solution were negligible. Calibration levels were prepared and were linear in the whole range tested

Table S3. Comparison of different analytical methods with the present study

Dust (mg, size)	Extraction	Clean-up	Evaporation/ reconstitution	Analysis	Conc. factor[a]	Ref.
100 mg, < 150 µm	2 steps with 5 mL methanol by orbital shaking (12 h) followed by centrifugation (4500 g, 10 min)	Oasis HLB catridges	Yes (prior and after clean-up). Final extract volume 0.25 mL water:methanol (40:60, v/v)	LC-(ESI) MS/MS	400	Li et al. 2019.
100 mg, < 125 µm	3 steps with 30 mL hexane:acetone (1:1 v/v) by vortexing (1 min) and ultrasonication (10 min) followed by centrifugation (3000 rpm, 10 min)	Florisil catridges	Yes (prior and after clean-up). Final extract volume 1 mL hexane: acetone (1:1 v/v)	GC-EI-MS/MS	100	Velázquez et al., 2018
30 mg, < 250 µm	3 steps with 2.5 mL hexane:acetone (3:1 v/v) by ultrasonication (10 min) and vortexing (1 min)	Aminopropyl silica cartridges	Yes (prior and after clean-up). Final extract volume 0.1 mL isooctane or methanol	GC-EI-MS and LC-(ESI) MS/MS for oligomeric OPFRs	300	Kademoglou et al., 2017
Sample size not specified, < 500 µm	3 steps with 2 mL hexane:acetone (3:1 v/v) by vortexing (1 min) and ultrasonication (5 min) followed by centrifugation (2000 g, 2 min)	Florisil catridges	Yes (prior and after clean-up). Final extract volume (nonane) not specified.	GC-EI-MS	-	De la Torre et al., 2020
100 mg, < 300 µm	Accelerated solvent extraction with dichloromethane (100 °C, 68 atm)	Size exclusion chromatography followed by a silica glass extraction column	Yes (prior and after clean-up steps and combined with solvent exchange). Final extract volume (methanol) not specified.	LC-(APPI) MS/MS	-	Percy et al. 2020
50 mg, < 500 µm	1 step SUPRAS extraction (0.2 mL 1-hexanol, 0.2 mL THF and 0.8 mL water) by vortexing (5 min) followed by centrifugation (10000 rpm, 20 min)	No	No (final extract volume 0. 37 mL)	LC-(APCI) MS/MS	135	Present study

[a]Concentration factor calculated as sample (mg)/final extract volume (mL)

(10 – 1,300 ng·g^{-1}, 500 ng·g^{-1} of IS, levels expressed in ng g^{-1} considering a sample amount of 50 mg) with R^2 that varied from 0.9841 to 0.9933. A calibration curve was prepared for TPHP and other one was prepared for BDP, CDP, EHDPP, IDPP and RDP. In this way, TPHP present as impurity in aryl-OPFRs standards (typically 0.5 - 5 % w/w) did not interfere in the quantitation of TPHP. It is worth mentioning that information about the relative abundance of the oligomers of IDPP, RDP and BDP was not given by the provider, so that quantitation was made on the basis of the oligomer *n*=1, which is expected to be the most abundant.

Three procedural blanks were run in each batch of experiments. We did not find detectable levels of aryl-OPFRs. We believe that the simplicity of the method (without several steps or additional clean-up) helped to prevent background contamination.

A certain degree of clean-up is achieved with SUPRAS treatment. It has been previously reported that SUPRAS feature restricted access properties due to both chemical interactions and the limited pores size in their network, so that interfering macromolecules, such as proteins, humic acids and polysaccharides, are not co-extracted. Furthermore, the equilibrium aqueous solution acts as a sink of polar interferents (Ballesteros-Gómez & Rubio, 2012). Accuracy (expressed as recovery, %) and precision (intra-day repeatability, RSD, *n*=3) were tested at three concentration levels (50, 360 and 1,300 ng g^{-1}). Results are shown in Table 1.

Accuracy was in the range 77 - 118% for all the target compounds with RSD between 0.6 and 19%. Method LODs (0.2 - 5 ng·g^{-1}) and LOQs (0.5-10 ng·g^{-1}) were estimated from a signal-to-noise ratio of 3 and 10, respectively (see Table S4).

Table 1. Recoveries of target compounds fortified at three different levels and blanks.

Analyte	Concentration ($ng \cdot g^{-1}$)	Recoveries (n=3)	RSD (%)	Blank
BDP	50	108 ± 15	14	n.d.
	360	89 ± 17	19	
	1,300	103 ± 9	9	
CDP	50	106 ± 11	10	n.d.
	360	107 ± 9	8	
	1,300	108 ± 13	12	
EHDPP	50	103 ± 6	6	n.d.
	360	101.9 ± 0.6	0.6	
	1,300	81 ± 3	4	
IDPP	50	115± 9	8	n.d.
	360	90 ± 5	6	
	1,300	77 ± 2	3	
RDP	50	87 ± 11	13	<LOQ
	360	90 ± 9	10	
	1,300	84 ± 7	8	
TPHP	50	77 ± 8	10	36 ± 7
	360	118 ± 14	12	
	1,300	93± 3	3	

Average recovery of IS [TPHP-d_{15} peak areas$_{spiked\ dust\ (average,\ n=9)}$ / TPHP-$d15_{calibration\ standads\ (average,\ n=7)}$] was 97±10 ng g^{-1}

Table S4. Analytical performance of the SUPRAS-based calibration[a]

	Slope (counts g ng^{-1}) ± SD	R^2	[b]LOD ($ng \cdot g^{-1}$)	LOQ ($ng \cdot g^{-1}$)
IDP	0.0077 ± 0.0002	0.9907	3	7
EHDPP	0.003 ± 0.0001	0.9857	3	9
TPHP	0.0058 ± 0.0003	0.9841	1	4
CDP	0.00101 ± $3 \cdot 10^{-5}$	0.9933	5	10
BDP	0.0151 ± 0.0005	0.9905	0.2	0.5
RDP	0.00171 ± $5 \cdot 10^{-5}$	0.9914	1	3

[a]IS mix at 500 ng/g, n=7, weight 1/x, origin included, calibration range: 10-1300 ng/g
[b]LOD (ng/g) reported in Li et al. 2019: CDP (1), IDP (0.31), EHDPP (0.39), TPP (0.4), RDP (0.74), BDP (0.52), 100 mg sample, dilution factor 1:4: our method: 50 mg sample, dilution factor ~1:4

Finally, matrix effects were not investigated, since total recoveries of target compounds (Table 1) were acceptable. Furthermore, the average internal standard recovery in the dust sample used for validation was 97±10 (Table 1) and values varied from 60 to 120% in samples (Table 2). Low matrix effects may be due to a combination of the SUPRAS treatment and the use of APCI instead of ESI for ionization. APCI has been reported to be a more selective ionization source for OPFRs (Amini & Crescenzi, 2003). In fact, although both GC-MS(EI) and LC-MS/MS(ESI) have been the most reported techniques for the analysis of OPFRs (Van de Veen et al. 2012), LC-MS/MS with APCI ionization has been claimed to be advantageous over ESI also in terms of better sensitivity (Tokumura et al. 2018; Ballesteros-Gómez et al. 2014).

Table 2. Levels of target compounds and IS recoveries in indoor dust from classrooms and houses (ng g^{-1}).

		Analytes							Recoveries
		BDP	CDP	EHDPP	IDPP	RDP	TPHP	∑aryl-OPFRs	IS (%)
Classrooms (n=16)	Concentration range	<LOD – 98	<LOD – 204	19 – 75,763	<LOD – 2,154	<LOD – 317	46 – 9,902	207 – 87,690	60 –107
	Mean	16	62	5,377	573	52	2,081	8,157	90
	Median	4	34	407	403	14	363	2,077	91
	DF (%)	44	69	100	94	81	100		
Houses (n=22)	Concentration range	<LOD – 2,235	<LOD – 776	<LOD – 4,299	<LOD – 1,271	<LOD – 166	<LOD – 7,998	<LOD – 8,153	73 – 120
	Mean	159	120	598	174	22	1,038	2,106	101
	Median	11	51	69	87	<LOQ	497	952	106
	DF (%)	59	73	59	86	50	86		

DF: Detection frequency.

3.2. Aryl-OPFRs concentrations in indoor dust.

Table 2 shows the concentration range, mean, median and detection frequency (DF) of the target compounds in each microenvironment. Figure 1 shows the relative abundance of the compounds in houses and classrooms. Levels measured in each sample are given in Tables S5 and S6.

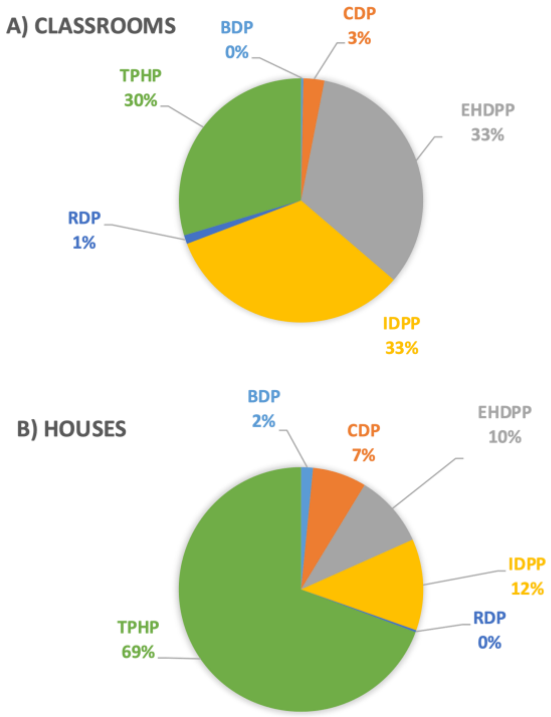

Figure 1. *Relative abundance of target aryl-OPFRs in classrooms and in houses*

When considering the sum of all monitored aryl-OPFRs (Σaryl-OPFRs) in houses (see table S5), median values varied between 34 ng·g^{-1} (for a non-habited house, no electronic appliances except wall plugs, suburban area) and 8,153 ng·g^{-1} (for an urban house, 2 inhabitants and one dog, 5-10 electronic appliances in the sampled room). Although minimum and maximum contamination levels were in accordance with the characteristics of these two locations, we could not find any clear trend when all the samples were examined (e.g. type of floor, paint, air conditioning, number of inhabitants, pets, etc. see table S7).

The median Σaryl-OPFRs was two times higher in classrooms than in houses and were lower for kindergartens (samples C1-C5, median 1,234 ng·g^{-1}) and primary schools (samples C6-C8, median 1,330 ng·g^{-1}) than for University classrooms (samples C11-C16, median 5,907 ng·g^{-1}) (see table S6). These results could be explained by a variety of different characteristics in both type of environments (table S8).

Table S5. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different houses.

	BDP	CDP	EHDPP	IDP	RDP	TPHP	Σaryl-OPFRs
H1$_b$	57	<LOQ	205	204	<LOD	1,794	2,260
H2$_b$	127	72	<LOD	108	3	549	860
H3$_b$	<LOD	136	333	99	<LOD	145	713
H4$_b$	<LOD	<LOD	<LOD	9	<LOD	274	283
H5$_b$	<LOD	<LOD	87	<LOD	<LOD	<LOD	87
H6$_l$	88	184	1,908	252	<LOD	986	3,419
H7$_l$	<LOD	189	138	225	5	163	721
H8$_l$	<LOD	30	<LOD	<LOD	<LOD	76	106
H9$_l$	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.00
H10$_l$	729	188	4,299	139	139	1,989	7,483
H11$_l$	18	103	223	68	7	266	685
H12$_l$	8	<LOD	<LOD	75	<LOD	4,117	4,200
H13$_l$	35	391	3,578	693	<LOD	1,076	5,773
H14$_l$	62	275	51	1,271	43	427	2,130
H15$_l$	67	776	<LOD	47	9	513	1,414
H16$_l$	11	<LOD	284	<LOQ	42	548	885
H17$_l$	2,235	110	788	134	166	481	3,914
H18$_l$	<LOD	<LOD	<LOD	34	<LOD	<LOD	34
H19$_l$	<LOD	<LOQ	1,226	22	14	56	1,318
H20$_l$	12	<LOQ	34	264	35	523	869
H21$_l$	25	102	<LOD	24	5	7,998	8,153
H22$_l$	<LOD	<LOQ	<LOD	151	<LOD	869	1,020

b: bedroom; l: living room

Table S6. Concentrations of target compounds (ng·g^{-1}) in dust samples collected from different classrooms.

	BDP	CDP	EHDPHP	IDPP	RDP	TPHP	Σaryl-OPFRs
C1$_k$	<LOD	<LOD	19	309	317	46	691
C2$_k$	37	180	75,763	1,783	27	9,902	87,690
C3$_k$	<LOD	53	399	57	104	194	808
C4$_k$	<LOD	<LOD	414	2,154	<LOD	170	2,738
C5$_k$	<LOD	<LOD	305	453	99	377	1,234
C6$_s$	<LOD	<LOD	260	24	62	2,522	2,868
C7$_s$	6	57	206	461	11	589	1,330
C8$_s$	<LOD	<LOD	31	69	75	102	277
C9$_h$	<LOD	<LOQ	190	<LOD	14	67	271
C10$_h$	<LOD	<LOQ	61	19	<LOD	127	207
C11$_u$	11	28	526	353	6	6,612	7,536
C12$_u$	41	204	1,014	822	12	6,263	8,357
C13$_u$	26	160	1,413	1,057	14	5,082	7,753
C14$_u$	7	40	1,424	909	<LOD	673	3,053
C15$_u$	<LOD	165	479	463	79	229	1,415
C16$_u$	98	58	3,535	228	12	349	4,279

k: kindergarten; s: (primary) school; h: high school; u: university.

Table S7. Characteristics of the houses

	Inhabitants	Furry pets	Type of floor	Air conditioning[a]	Nº electronic appliances	Location
H1$_b$	3	0	Slabs or tiles	no	<5	rural
H2$_b$	4	0	Slabs or tiles	yes	>10	rural
H3$_b$	3	0	Slabs or tiles	no	<5	rural
H4$_b$	3	0	Slabs or tiles	no	<5	rural
H5$_b$	1	0	Slabs or tiles	no	<5	urban
H6$_l$	4	0	Slabs or tiles	no	5 y 10	rural
H7$_l$	3	0	Slabs or tiles	no	5 y 10	rural
H8$_l$	3	1	Slabs or tiles	yes	5 y 10	rural
H9$_l$	3	0	Slabs or tiles	yes	<5	rural
H10$_l$	4	0	Slabs or tiles	no	5 y 10	rural
H11$_l$	4	0	Slabs or tiles	yes	<5	rural
H12$_l$	5	0	Slabs or tiles	yes	<5	urban
H13$_l$	3	1	Slabs or tiles	yes	<5	rural
H14$_l$	4	0	Slabs or tiles	yes	>10	urban
H15$_l$	3	2	Slabs or tiles	yes	5 y 10	urban
H16$_l$	2	1	wood laminate	yes	>10	suburban
H17$_l$	2	1	wood laminate	yes	>10	suburban
H18$_l$	0	0	Slabs or tiles	no	0	urban
H19$_l$	2	0	Slabs or tiles	yes	5 y 10	urban
H20$_l$	4	0	Slabs or tiles	yes	5 y 10	urban
H21$_l$	2	1	Slabs or tiles	no	5 y 10	urban
H22$_l$	2	1	Slabs or tiles	yes	5 y 10	urban

b: bedroom; l: living room; [a]ventilation trough windows is frequent in all houses; rural means from villages of ≤10,000 inhabitants in Córdoba province; suburban: surroundings of Córdoba city

Table S8. Characteristics of the classrooms

	Type	Capacity (persons)	Type of floor	Air conditioning	Windows used for ventilation	Location
C1	Kindergarten	10	Plastic laminate	yes	yes	rural
C2	Kindergarten	20	Plastic laminate	yes	yes	rural
C3	Kindergarten	21	Plastic laminate	no	yes	rural
C4	Kindergarten	16	Plastic laminate	no	yes	rural
C5	Kindergarten	18	Plastic laminate	no	yes	rural
C6	Primary School	20	Slabs or tiles	no	yes	rural
C7	Primary School	13	Slabs or tiles	no	yes	rural
C8	Primary School	20	Slabs or tiles	no	yes	rural
C9	High School	12	Slabs or tiles	yes	yes	rural
C10	High School	15	Slabs or tiles	yes	yes	rural
C11	University	80	Plastic laminate	yes	no	suburban
C12	University	80	Plastic laminate	yes	no	suburban
C13	University	30	Plastic laminate	yes	no	suburban
C14	University	80	Slabs or tiles	yes	no	suburban
C15	University	80	Plastic laminate	yes	no	suburban
C16	University	30	Slabs or tiles	yes	yes	suburban

Rural means from villages of ≤10,000 inhabitants in Córdoba province; suburban: surroundings of Córdoba city

First, the room capacity of the University classrooms was higher (~80-100 persons) than in kindergartens and primary schools (~10-20 persons). We also observed the presence of different building materials, such as laminated plastic flooring was present at the University classrooms and slabs or tiles at kindergartens and primary schools. The use of electronic equipment was more frequent at the University (video projector, laptops, mobile phones, etc.) and classrooms had air conditioning (no windows) while most of kindergartens and primary schools did not have air-conditioning but windows were daily opened for ventilation. Finally, the age of the building could be another influential factor but we

could not gather specific construction dates. Education buildings were all approximately between 10 and 30 years old and they were all refurbished/renovated at least once. The University classrooms were around 20 years old.

The most abundant aryl-OPFR in houses was TPHP with a median concentration of 497 ng·g^{-1} (DF 86%). In terms of relative abundance, it accounted for 69% in houses (followed by 12% IDPP, 10% EHDPP and 7% CDP) (see Figure 1). Differently, EHDPP and IDPP were the most abundant aryl-OPFRs in classrooms with median concentrations of 407 ng·g^{-1} (DF 100%) and 403 ng·g^{-1} (DF 94%), respectively, followed by TPHP (median 363 ng·g^{-1}, DF 100%). The relative abundance of EHDPP and IDPP in classrooms was ~33%. Statistical tests did not show significant differences between houses and classrooms in levels of TPHP ($p=0.667$) and EHDPP ($p=0.250$). Contrarily, values of IDPP differed significantly ($p=0.017$).

The ubiquitous presence of TPHP is explained by the fact that it is the most widely produced and used OPFR in European countries (Van der Veen and de Boer., 2012) and in addition, it is an impurity of other aryl-OPFRs (Kademoglou et al. 2017). TPHP is widely used as flame retardant and plasticizer in a variety of products, including cellulose nitrate, various coatings, triacetate film and sheet, rigid urethane foam and engineering thermoplastics such as poly(p-phenylene) oxide (PPO)/high impact polystyrene (HIPS) and acrylonitrile-styrene-butadiene (ABS)-polycarbonate (PC) blends (Weil 1993). It is also applied in roofing paper, lacquers, varnishes and in vinyl automotive upholstery (WHO 1991).

TPHP is usually the most abundant aryl-OPFR in indoor dust and it has been widely reported in house dust from European countries at median levels that are in agreement with those found in this study, namely 544 ng·g^{-1} (Greece, Li et al, 2019), 203 ng·g^{-1} (Romania, Li et al, 2019), 1,509 ng·g^{-1} (UK, Kademoglou et al., 2017), 1102 ng·g^{-1} (Spain, Barcelona, Cristale et al., 2016), 369 ng·g^{-1} (Spain, Barcelona, Velázquez-

Gómez et al., 2019), 744-944 ng·g^{-1} (Spain, Córdoba, Björnsdotter et al., 2018). Cristale et al. (2016) reported a similar median level of TPHP in schools from Barcelona (604 ng·g^{-1}) than that measured in classrooms in our study (363 ng·g^{-1}). Higher levels have been reported by other authors, e.g. 3,011 ng·g^{-1} in high schools in Spain (Barcelona, Velázquez-Gómez et al., 2019) and 4,100 ng·g^{-1} in primary schools and child daycare centers from UK (Brommer and Harrad, 2015).

EHDPP and IDPP, the most abundant compounds in classrooms in our study, are applied in flexible polyvinyl chloride (PVC) (Van der Veen and de Boer, 2012). PVC is widely used in construction materials such as pipes, wires and cables, power supplies, decorative laminating films and sheets in floors, roofs, doors, fittings in windows frames, blinds, power supplies, appliances, car interiors, etc. (Ciacci et al., 2017). A possible explanation for our findings is that these type of PVC materials could be more frequently used in classrooms than in houses. However, EHDPP and IDPP are applied in many other types of materials too. EHDPP is added to cellulose and cellulose copolymers, polymethyl methacrylate and polystyrene and it can also be found in rubber, photo films, paints, pigment dispersions, adhesives and textile coatings including food packaging applications (Brooke et al., 2009a). IDPP can be also employed in synthetic rubber, textiles and pigment products (Kademoglou et al. 2017). We analysed materials from a representative University classroom (sample C11, Table S6) and results revealed considerable amounts of IDPP, EHDPP and TPHP. Contamination was mainly detected in samples collected from the plastic floor (laminate and fittings, most probably made up of PVC).

Brommer and Harrad (2015) also found significantly higher levels of EHDPP in classrooms (median 29 μg g^{-1}) than in houses (median 1,600 ng·g^{-1}) (samples collected in UK). The same trend was observed by Velázquez-Gómez et al. (2019) in high schools classrooms from Barcelona (median 1,954 ng·g^{-1}) in comparison with houses (median 289 ng·g^{-1}). However, Cristale et al. (2016) reported a higher median value of EHDPP

in houses (1,262 ng·g^{-1}) than in schools (772 ng·g^{-1}). Levels of IDPP in classrooms have not been reported yet. IDPP was first reported in indoor dust by Kademoglou et al. (2017) being the most abundant OPFR in UK and Norwegian house dust, with median levels of 401 and 51.3 ng·g^{-1}, respectively. Lower median values of IDPP have been reported in house dust from Greece (10.9 ng·g^{-1}) and from Romania (16.8 ng·g^{-1}) by Li et al (2019), which are in the same order of magnitude than the levels measured in this study (median 87 ng·g^{-1}). We measured the highest values of EHDPP (76 μg g^{-1}) and IDPP (2 μg g^{-1}) in two kindergartens where plastic floor, shelves, mats and toys were abundant and some electronic equipment (TV, audio) was also present.

CDP is used also in a variety of products as textile coating, lubricants additives, adhesives, in PVC applications, in thermoset resins, in thermoplastics and in polyurethane (Brooke et al., 2009b). Median values in house dust from Greece and Romania were 59.9 and 100 ng·g^{-1}, respectively, which are in line with those measured in Spanish houses from Córdoba (median 51 ng·g^{-1}). Values of CDP in Spanish classrooms (median 34 ng·g^{-1}) were not significantly different than in houses ($p=0.522$). To the best of our knowledge, this is also the first study reporting the presence of this novel aryl-OPFR in classrooms.

Studies on the presence of oligomeric OPFRs in dust are still more limited than on monomeric OPFRs but they are increasing in the last years. RDP and BDP are considered Deca-BDE alternatives for use in electronic products (Lowell Center for Sustainable Production, 2005) and their use is expected to increase accordingly. They have lower volatility and higher environmental stability than monomeric OPFRs (Van der Veen and de Boer, 2012). They are mainly applied in thermoplastics [RDP is used in ABS and in PC/ABS and PPO/ HIPS blends and BDP in HIPS, PC, PPO and PC/ABS blends (Roth et al., 2012)]. Median levels of BDP and RDP in Spanish houses were 11 ng·g^{-1} for BDP and below the quantification limit for RDP (DF 59 and 50%, respectively). These values are in accordance with those reported in the recent literature. So, mean

levels of BDP and RDP were below the detection limit in houses from Romania (DF 35 and 43%, respectively) (Li et al., 2019). In houses from Greece, the mean value of RDP was also below the detection limit (DF 37%) while the median of BDP reached 12.8 ng·g^{-1} (DF 83%). In UK houses median levels of BDP and RDP were 55 ng·g^{-1} (DF 50%) and 1.9 ng·g^{-1} (DF 100%), respectively (Kademoglou et al., 2017). To the best of our knowledge, there are not reported studies on RDP and BPD in classrooms. While we found similar levels of BPD in classrooms (median 4 ng·g^{-1}, DF 44 %) than in houses, RDP levels and its DF were higher in classrooms (median 14 ng·g^{-1}, DF 81 %). The highest value of RDP (317 ng·g^{-1}) was measured in a kindergarten while the highest value of BDP (98 ng·g^{-1}) was reported in a University classroom. Accordingly, statistical tests showed significant differences in the levels of RDP measured in classrooms and in houses ($p=0.026$) and no significant differences in the levels of BPD ($p=0.194$).

Finally, it is worth mentioning that samples were collected in spring and that some authors have reported different seasonality in the levels of the most volatile OPFRs due to temperature increase, which could enhance their release from materials. Cao et al. 2014 measured higher levels in late winter and early spring while Chen et al. 2019 measured higher levels in summer. Nevertheless, other factors like building ventilation (windows or air conditioning) or wet deposition may influence this behavior (Chen et al. 2019). Furthermore, less volatile compounds, like RDP and BDP, may not follow these trends.

3.3. Correlation between target compounds

Taking into account all the samples, statistically significant positive correlations between aryl-OPFRs were found for half of the tests ($0.3 < \rho < 0.6$, $p<0.05$) (indicated in bold in Table S9). For the other half, correlations were positive ($0.07 < \rho < 0.2$) but no statistically significant

(p>0.05). These results indicate similar sources of origin and applications in products (Li et al., 2019).

Table S9. Spearman correlation values and their respective p-values for each couple of flame retardants in all microenvironments. Highlighted values are statistically significant (p<0.05) and show positive correlations (r>0).

	All samples n= 53	p-value	Classrooms n= 16	p-value	Houses n= 22	p-value
BDP-CDP	**0.6**	**0.0001**	**0.7**	**0.001**	**0.6**	**0.008**
BDP-EHDPP	0.1	0.4	0.3	0.3	0.03	0.9
BDP-IDPP	**0.3**	**0.04**	0.5	0.07	**0.5**	**0.03**
BDP-RDP	0.07	0.6	0.4	0.1	**0.4**	**0.05**
BDP-TPHP	**0.6**	**0.0001**	**0.7**	**0.02**	**0.7**	**0.004**
CDP-EHDPP	0.1	0.4	0.4	0.2	0.3	0.3
CDP-IDPP	**0.4**	**0.01**	0.5	0.08	**0.6**	**0.005**
CDP-RDP	0.1	0.5	0.1	0.7	0.3	0.1
CDP-TPHP	**0.4**	**0.02**	0.5	0.1	0.4	0.1
EHDPP-IDPP	**0.4**	**0.04**	0.4	0.2	0.3	0.2
EHDPP-RDP	**0.4**	**0.02**	0.2	0.6	0.4	0.08
EHDPP-TPHP	0.1	0.6	0.7	0.06	0	1
IDPP-RDP	0.2	0.3	0.1	0.7	0.1	0.7
IDPP-TPHP	**0.6**	**0.003**	**0.7**	**0.03**	**0.6**	**0.008**
RDP-TPHP	0.1	0.8	0.3	0.3	0.3	0.2

TPHP was highly correlated with BDP and with IDPP ($0.6 < \rho < 0.7$, $p \leq 0.003$) in all the samples and in houses and moderately correlated ($r=0.7$, $p<0.05$) in classrooms. TPHP was moderately correlated with CDP in all samples ($r=0.4$, $p<0.05$). These correlations are probably due to the fact that TPHP is an impurity of these compounds and this is in agreement with results from Li et al (2019). Furthermore, it has been reported that TPHP could be used in combination with RDP and BDP to improve flame retardancy (Levchik and Weil et al., 2006). TPHP has been reported in technical mixtures of OPFRs at percentage levels of 1.5-≤4 in EHDPP, 25% in CDP, ≤5-6 in IDPP, 1-2% in RDP and 4-33% in BDP (Brooke et al., 2019c). Although TPHP is an impurity of all aryl-OPFRs, we did not find significant correlations with RDP and EHDPP.

CDP was significantly correlated with BDP ($0.6 < \rho < 0.7$, $p<0.01$) in all cases. This correlation was also observed by Li et al. (2019) with a value of 0.6 ($p<0.01$). This may suggest a similar application pattern of both compounds. IDPP was also moderately correlated with BDP and with CDP ($0.3 < \rho$ 0.6, $p<0.05$) in all the samples and in houses. BDP was

correlated with RDP (r=0.4, p=0.05) only in houses. Differences between microenvironments may indicate the predominance of different products and materials in houses and in classrooms, such as different thermoplastics products, electronic products, etc.

3.4. Human exposure via dust ingestion.

The exposure pathway via dust ingestion was estimated, as one of the main routes of human exposure to these compounds (Wei et al. 2015, Ali et al. 2013, Jones-Otazo et al. 2005). The following equation was employed and adapted to the sampled microenvironments (US, EPA, 1997):

$$Daily\ Exposure\ \left(\frac{\text{ng/kg bw}}{\text{day}}\right) = \frac{(Ch\ x\ R\ x\ Eh) + (Cc\ x\ R\ x\ Ec)}{Body\ weight}$$

where C is the concentration in houses (C_h) and in classrooms (C_c), R is the dust ingestion rate and E is the exposure duration. Eh is the percentage of time spent in each place, evaluated in 24 h. E was set at 8h at work (Ec) and 16h at home (Eh) for adults and at 6h at kindergarten (Ec) and 18h at home (Eh) for toddlers. For toddlers who stay at home Eh was 24 h. Body weight was 70 kg and 12.3 kg for adults and toddlers, respectively. We considered two possible scenarios of exposure (average and worst-case). In the average case, R was 20 mg·day^{-1} for adults and 50 mg·day^{-1} for toddlers, and in the worst case, R was 50 mg·day^{-1} for adults and 200 mg·day^{-1} for toddlers (Brandsma et al., 2013).

We studied four population groups: students/workers at University, teachers/workers at kindergartens, toddlers that go to kindergartens and toddlers that stay at home. We did not make estimations related to other education buildings due to the limited number of samples.

Table 3 shows the estimated daily intakes (EDIs) via dust ingestion (ng·kg bw^{-1}·day^{-1}) for these four groups. As expected, toddlers were 12-18 times more exposed to the sum of aryl-OPFRs than adults (when comparing toddlers that go to kindergartens with workers at these education buildings). Toddlers spend long time playing on indoor floors and show frequent hand-to-mouth contact (Lewis et al. 1994) so that higher dust ingestion rates are estimated (50-100 mg dust day^{-1}) and consequently, also higher exposure levels which are enhanced by their low body weight.

When comparing subgroups, toddlers that go to kindergartens would be as exposed to ∑aryl- OPFRs than those that stay at home. Contrarily, workers at kindergartens were 2-2.5 less exposed to aryl-OPFRs than workers and students at Universities (considering both median and maximum levels).

Regarding the EDIs of the individual compounds (average scenario), toddlers that go to kindergartens are ≥2 times exposed to EHDPP, IDPP and RDP. The same trend is observed between workers at kindergartens and at Universities. Contrarily, workers at Universities are around 3 times more exposed to TPHP. All these differences become minor when maximum EDI levels are compared.

TPHP and EHDPP are the most frequently studied aryl-OPFRs and there are many reports that estimate EDIs from indoor dust collected in houses. For toddlers that stay at home, EDIs (median) were 2 ng·kg^{-1}·day^{-1} (average) and 8 ng·kg^{-1}·day^{-1} (worst case) for TPHP and 0.2 ng·kg^{-1}·day^{-1} (average) and 1 ng·kg^{-1}·day^{-1} (worst case) for EHDPP. These results were in accordance with the recent study of Li et al. (2019) with EDIs that were in the ranges 0.03-1.1 ng·kg^{-1}·day^{-1} and 0.19-36 ng·kg^{-1}·day^{-1} for TPHP in average and worst cases, respectively, and 0-0.23 ng·kg^{-1}·day^{-1} and 0.04-2.23 ng·kg^{-1}·day^{-1}for EHDPP in average and worst cases, respectively.

Table 3. Estimated exposure to aryl-OPFRs via dust ingestion (ng·kg bw^{-1}·day^{-1}) in toddlers and adults.

		Toddlers that go to kindergartens		Toddlers that stay at home		Workers in kindergartens		Workers or students at Universities	
		Average	High	Average	High	Average	High	Average	High
Median	**BDP**	0.04	0.15	0.05	0.18	0.00	0.01	0.00	0.01
	CDP	0.16	0.62	0.21	0.83	**0.01**	0.02	0.02	0.05
	EHDPP	0.62	2.46	0.28	1.12	**0.05**	0.13	0.13	0.32
	IDPP	0.73	2.90	0.35	1.41	0.06	0.14	0.08	0.19
	RDP	0.11	0.43	0.01	0.03	0.01	0.02	0.00	0.00
	TPHP	1.71	6.85	2.02	8.08	0.11	0.28	0.37	0.92
	∑aryl-OPFRs	3.35	13.42	2.92	11.66	0.25	0.61	0.60	1.50
Maximum	**BDP**	6.85	27.41	9.09	36.34	0.43	1.08	0.44	1.09
	CDP	2.55	10.20	3.16	12.63	0.17	0.41	0.17	0.42
	EHDPP	20.36	81.43	17.48	69.91	1.50	3.74	1.16	2.89
	IDPP	6.06	24.25	5.17	20.66	0.45	1.12	0.34	0.86
	RDP	0.83	3.31	0.67	2.70	0.06	0.15	0.04	0.10
	TPHP	34.45	137.78	32.51	130.04	2.47	6.16	2.15	5.39
	∑aryl-OPFRs	71.10	284.39	68.07	272.27	5.07	12.66	4.30	10.75

Studies on EDIs that take into account the time spent in education buildings are scarce. Median EDIs for toddlers that go kindergartens were 1.7 and 0.6 ng·kg^{-1}·day^{-1} (average case) and 9 and 2.5 ng·kg^{-1}·day^{-1} (worst case) for TPHP and EHDPP, respectively. These values were lower than in other studies, e.g. 7 and 360 ng·kg^{-1}·day^{-1} (UK, Brommer et al. 2015) and 14 and 56 ng·kg^{-1}·day^{-1} (Brazil, Cristale et al. 2018) for TPHP (average and worst cases). Levels for EHDPP (average and worst cases) were 14 and 420 ng·kg^{-1}·day^{-1} (Brommer et al. 2015) and 12 and 48 ng·kg^{-1}·day^{-1} (Cristale et al. 2018).

EDIs (median) for workers at kindergartens were 0.1 and 0.3 ng·kg^{-1}·day^{-1} in average and worst cases, respectively for TPHP, and 0.05 and 0.1 ng·kg^{-1}·day^{-1} in average and worst cases, respectively, for EHDPP. EDIs (median) for workers or students at University were 0.4 and 0.9 ng·kg^{-1}·day^{-1} for TPHP and 0.1 and 0.3 ng·kg^{-1}·day^{-1} for EHDPP (average and worst cases). These values were similar than EDIs reported by Velázquez et al. (2019) for adults at high schools (TPHP: 0.44-1.1 ng·kg^{-1}·day^{-1}, EHDPP: 0.30-0.76 ng·kg^{-1}·day^{-1}).

In terms of novel aryl-OPFRs (IDPP and CDP), EDIs in both toddlers groups (0.4 - 3 ng·kg^{-1}·day^{-1} for IDPP and 0.15-0.8 ng·kg^{-1}·day^{-1} for CDP) were within the range of levels calculated by Li et al. (2019), i.e. 0.01 -14 ng·kg^{-1}·day^{-1} for both IDPP and for CDP. Regarding adults working at education buildings, EDIs for IDPP (0.05-0.85 ng·kg^{-1}·day^{-1}) were lower to EDIs reported by Kademoglu et al. (2017) for adults working at stores (0.6 and 35.4 ng·kg^{-1}·day^{-1}). However, they were in the same range than EDIs reported for adults that stay 24h at home (0-1.2 ng·kg^{-1}·day^{-1}, Kademoglu et al., 2017, Li et al., 2019).

EDIs for oligomeric aryl-OPFRs (BDP and RDP), which were at the lowest median levels in dust, were of 0.04-27.4 and 0.008-3.3. ng·kg^{-1}·day^{-1} of BDP and RDP for toddlers and 0.003-1.1 and 0.001-0.1 ng·kg^{-1}·day^{-1} of BDP and RDP for adults. Results were higher for BPD and similar or lower for RDP than those reported by Li et al. (2019), namely 0-1.35 and 0-0.5

ng·kg^{-1}·day^{-1} for BDP and RDP in toddlers and 0-0.31 and 0-1.1 ng·kg^{-1}·day^{-1} for BDP and RDP in adults.

In all cases, the calculated exposure levels were much lower than the reported levels of Reference Doses (RfD), being 7·10^{4} ng·kg^{-1} (Li et al. 2018), 6·10^{6} ng·kg^{-1} (UK Environment Agency, 2009c) and 9.3·10^{6} ng·kg^{-1} (UK Environment Agency, 2009b) for TPHP, EHDPP and IDPP, respectively. Nevertheless, these substances are still of concern for the human health and the environment, since many toxic properties (neurotoxicity, developmental toxicity, damage to the reproductive function, endocrine disruption, etc.) and, sometimes high persistence and high bioaccumulation potential, have been reported by authors (Wei et al. 2015, Yang et al. 2019, Du et al. 2015, Waaijers et al., 2012) and by technical reports (Table S1).

4. Conclusions

A SUPRAS-based method was validated for generic sample treatment of different aryl-OPFRs in indoor dust. SUPRAS extraction and clean-up (exclusion of macromolecules and polar interferents) occurred in a single step. The method was advantageous in terms of simplicity and rapidity over reported strategies (5 min stirring and centrifugation without further additional clean-up or evaporation steps). Dust samples from houses and education buildings from Spain were analysed. TPHP was the most abundant aryl-OPFR in houses while EHDPP and IDPP were the most abundant in education buildings. Median levels of ∑aryl-PFRs were 2 times higher (207-87,690 ng g^{-1}) in classrooms than in houses (<LOD-8,153 ng g^{-1}). We could not find clear trends between levels and the characteristics of the sampled rooms (ventilation, room capacity, materials, etc.). IDPP (median 403 ng g$^{-1,}$ DF 94%),

RDP (median 14 ng $g^{-1,}$ DF 81%) and BDP (median 4 ng $g^{-1,}$ DF 44%) were detected for the first time in classrooms. In terms of human exposure to ∑aryl-PFRs via dust ingestion, values were not different for toddlers that stay at home than for those who go to kindergartens. University workers and students were the most exposed to aryl-OPFRs in comparison with other education centers.

Conflict of interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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Characterization of a new sustainable supramolecular solvent and application to the determination of oxy-PAHs in meat, seafood and fish tissues

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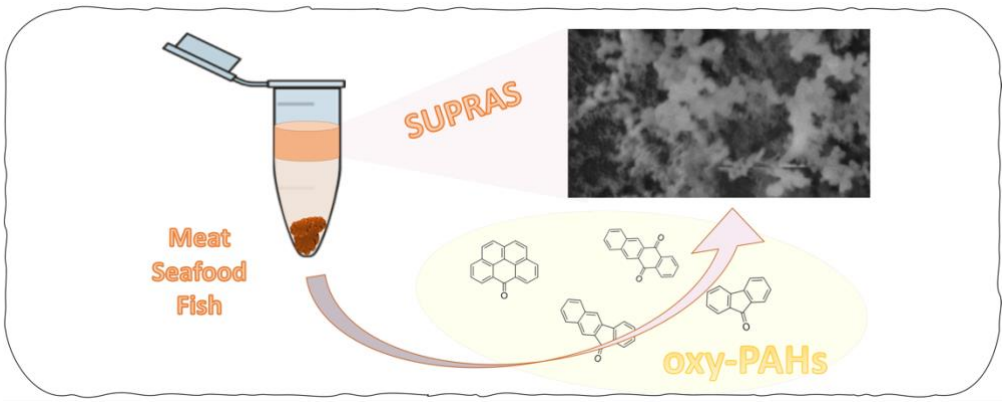

Highlights

- New green SUPRAS made up fatty alcohols, water and 2-MeTHF are characterized.
- They were successfully applied to the extraction of oxy-PAHs from food.
- Method was fast (30 min) and with low consumption of solvent (200 µL SUPRAS).
- Meat, fish and seafood samples were contaminated with oxy-PAHs (n.d. - 8 ng/g).

Abstract

In this study we develop a green treatment method based on supramolecular solvents (SUPRASs) made up of reverse aggregates of short/medium chain length alcohols (C_6-C_{10}) in mixtures of water and a sustainable organic solvent (methyl-tetrahydrofuran). SUPRASs ingredients have low toxicity and can be obtained from renewable sources. The new SUPRASs were characterized and its suitability for determination of oxygenated polycyclic aromatic hydrocarbons (oxy-PAHs) in food was tested. Analysis was made by liquid chromatography coupled to high resolution mass spectrometry. The method provided quantification limits in the range 0.4 - 4 ng g^{-1} with low consumption of reagents (200uL of SUPRAS per sample) and it was based on simple agitation and centrifugation without concentration/evaporation steps. All target compounds (except 11-H-benzo[b]fluoren-11-one) were found in 7 out of 19 samples, mainly in fish and seafood samples, with levels in the range n.d. – 8 ng g^{-1}.

Keywords: *oxy-PAHs; emerging contaminants; supramolecular solvents; high resolution mass spectrometry; food samples; microextraction.*

Chemical compounds studied in this article naphtacene-5,12-dione (PubChem CID: 68179800); 6H-benzo[cd]pyren-6-one (PubChem CID:18310); 11H-benzo[b]fluoren-11-one (PubChem CID: 18311), 9H-fluoren-9-one (PubChem CID: 10241). More information.

1. Introduction

Oxygenated polycyclic aromatic hydrocarbons (oxy-PAHs) are derivatives from PAHs, which have one or more oxygen atoms in their structure (ketones, quinones, carboxaldehydes, carboxylic acids and lactones) (Clergé, Le Goff, Lopez, Ledauphin & Delépée, 2019). They are considered to be as toxic or even more toxic than their parents PAHs mainly due to both mutagenic potential (linked to cancer) and increased bioavailability (Clergé et al., 2019; Andersson & Achten, 2015; Yu, 2002). They are also suspected endocrine disrupting chemicals (Sidhu et al., 2005, Kishikawa et al., 2004). Oxy-PAHs can directly originate from the incomplete combustion of organic matter, coal or oil at temperatures above 500ºC (Layshock, Wilson & Anderson, 2010) or from the degradation of PAHs through chemical, enzymatic and biological transformation and they can bioaccumulate in organisms (Clergé et al., 2019; Lundstedt et al., 2007, De Witte, Walgraeve, Demeestere & Van Langenhove, 2019; Webster et al., 2011; Ranjbar Jafarabadi et al., 2019).

Despite of the need to elucidate the risk of the human exposure to oxy-PAHs, studies about their presence in environmental samples, and especially in food, is still limited. Results show that they are widely distributed in the atmosphere, water, soil and sediments at levels in the same order of magnitude than PAHs and up to 10 times higher than nitro-PAHs (Wei et al., 2015; Bandowe & Nkansah, 2016; De Oliveira et al., 2018). Table S1 shows reported levels in food, which range from few ng g^{-1} down to pg g^{-1} levels, together with details of the employed analytical methods for their determination.

Table S1. Reported presence of oxy-PAHs in food: target compounds, concentration range (ng·g^{-1}), detection (LOD) and quantification (LOQ) limits (ng·g^{-1}), sample type, sample preparation method and analysis technique

[a]Analytes	Levels (Σ, ng·g^{-1})	LOD (ng·g^{-1})	LOQ (ng·g^{-1})	Sample (n°)	Sample preparation	Anal	Ref
Benzo[a]anthracene-7,12-dione; **naphtacene-5,12-dione (DF: 88.89%); 9H-fluoren-9-one (DF: 77.78%); anthracene-9,10-dione (DF: 100%); naphthalene-1-ol (DF: 100%); benzanthrone (DF: 77.78%)**	12.6 – 32.97 (w.w.)	0.08 – 3.57	0.25 – 10.7	Mussel tissue (9)	PLE - SPE **Solvent:** hexane:acetone 3:1 (~40 mL/sample); **extraction time:** ~30min; **clean-up** (silica) **evaporation/reconstitution steps:** yes	LC-MS	1
Acenapthenequinone; aceanthracenequinone; phenanthrene-1,4-quinone; benzo[c]phenanthrene[1,4]quinone; 1,4-anthraquinone; **9H-fluoren-9-one ;** 4H-cyclopenta[d,e,f]phenanthren-4-one; 9,10-phenthrenequinone; **anthracene-9,10-dione**; **benzo[a]fluorenone**; **benzanthrone**; benzo[a]anthracene-7,12-dione; **naphtacene-5,12-dione**; 6H-Benzo[cd]pyren-6-one	282.1 (d.w.)	0.5-500 (pg)	-	Mussel tissue (SRM no.2977)	PLE – SPE **Solvent:** dichloromethane (~50 mL/sample); **extraction time:** 18min; **clean up** (size exclusion chromatography and silica SPE); **evaporation/reconstitution steps:** yes	GC-MS	2
1-indanone; 1,4-naphthoquinone; 1-naphthaldehyde; 2-biphenylcarboxaldehyde; 9H-fluoren-9-one; acenapthenequinone; anthracene-9,10-dione; 1,8-naphthalic anhydride; 4H-cyclopenta[d,e,f]phenanthren-4-one; 2-methyl-anthraquinone; benzo[a]fluorenone; benzanthrone; benzo[a]anthracene-7,12-dione; naphtacene-5,12-dione; 6H-Benzo[cd]pyren-6-one	Muscle: 28 - 1715 (d.w.) Gut: 317 - 836 (d.w.)	-	0.3 - 5	Demersal fishes (Drapane africana, Cynoglossus senegalensis, Pomadasys peroteti) (30)	PLE – SPE **Solvent:** dichloromethane (~40 mL/sample); **extraction time:** 12 min; **clean up** (silica/alumina chromatography column); **evaporation/reconstitution steps:** yes	GC-MS	3
-	Muscle: 40.67 - 80.34 (d.w.) Liver: 40.35 – 110 (d.w.)	-	-	Fishes (Lutjanus argentimaculatus, Lethrinus microdon and Scomberomorus guttatus)	PLE – SPE **Solvent:** dichloromethane (~68 mL/sample); **extraction time:** 12 min; **clean up** (silica SPE); **evaporation/reconstitution steps:** yes	GC-MS	4
9H-fluoren-9-one (DF: 100%); anthracene-9,10-dione (DF: 100%); benzanthrone (DF: 100%); benzo[a]anthracene-7,12-dione (DF: 100%)	8.5 - 80 (w.w.)	2.9 - 6.8	-	Smoked pork meat (2)	MARS – LLE – SPE **Solvent:** acetonitrile (25 mL/sample, MARS) and n-hexane (60 mL/sample, LLE); **extraction time:** 20 min (MARS); **clean up** (silica/alumina chromatography column); **evaporation/reconstitution steps:** yes	GC-MS	5
Anthracene-9,10-dione, benzo[a]anthracene-7,12-dione, benzanthrone, 11-B(b)fluo, 6H-Benzo[cd]pyren-6-one, 9,10-dihydro-8H-benzo[a]pyren-7-one**, 9H-fluoren-9-one, naphtacene-5,12-dione**	26 – 62.4 (w.w.)	0.04 – 0.43	0.12 - 1.43	Beef meat (12)	PLE – SPE **Solvent:** acetonitrile:ethyl acetate 1:3 (34 mL/sample); **extraction time:** 10 min; **clean up** (Dual Florisil + C18); **evaporation/reconstitution steps:** yes	GC-MS	6

Anthracene-9,10-dione (DF: 94%)	<1 – 3.2 (w.w.)	0.3	1	Frankfurt sausages (16)	PLE – SPE **Solvent:** n-hexane (68 mL/sample); **extraction time:** 20 min; **clean up** (Supelclean™ EZ-POP NP); **evaporation/reconstitution steps:** yes	GC-MS	7
9H-fluoren-9-one (DF: 100%); anthracene-9,10-dione (DF: 100%); Benzo[a]anthracene-7,12-dione (DF: 100%); Benzanthrone (DF: 100%)	40.70 - 47.26 (w.w.)	-	-	Waste cooking soybean oil (3)	LLE – SPE **Solvent:** acetonitrile:acetone 3:2 (36 mL/sample); **extraction time:** 31.5 min; **clean up** (Welchrom® C18E column + Welchrom® Florisil PR column); **evaporation/reconstitution steps:** yes	GC-MS	8
Anthracene-9,10-dione (DF: 100%); 9H-fluoren-9-one (DF: 100%); benzo[a]anthracene-7,12-dione (DF: 100%); benzanthrone (DF: 100%)	1.34 - 39.60 (w.w.)	0.03 – 0.08	0.09-0.24	Waste cooking soybean oil (15)	LLE – SPE **Solvent:** acetonitrile:acetone 3:2 (26 ml/sample); **extraction time:** 25 min; **clean up** (C18E SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	9
9H-fluoren-9-one (DF: 100%); anthracene-9,10-dione (DF: 100%); benzanthrone (DF: 87.5%); Benzo[a]anthracene-7,12-dione (DF: 75%); 9,10-dihydrobenzo[a]pyren-7(8H)-one (DF: 75%)	Soybean oil: 2.04 – 20.04 (w.w.) Rapeseed oil: 2.03– 6.56 (w.w.)	-	-	Soybean and rapeseed oil (8)	LLE – SPE **Solvent:** acetonitrile:acetone 3:2 (36 ml/sample); **extraction time:** 63 min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	10
9H-fluoren-9-one (DF: 100%); anthracene-9,10-dione (DF: 100%); benzo[a]anthracene-7,12-dione (DF: 100%); benzanthrone (DF: 83.3%); 9,10-dihydrobenzo[a]pyren-7(8h)-one (DF: 100%)	Soybean oil: 2.04 – 11.26 (w.w.) Rapeseed oil: 0.93– 10.88 (w.w.)	0.005 – 0.36	-	Soyabean and rapeseed oil (2)	LLE - SPE **Solvent:** acetonitrile:acetone 3:2 (36 mL/sample); **extraction time:** 63 min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	11
9H-fluoren-9-one; anthracene-9,10-dione; Benzo[a]anthracene-7,12-dione; Benzanthrone; 9,10-dihydrobenzo[a]pyren-7(8H)-one	flavouring oil gravy: 12.68 -12.13 (w.w.)	-	-	Flavouring oil gravies (300)	LLE -SPE **Solvent:** n-hexane and acetonitrile:acetone 3:2 (1 L/sample); **extraction time:** 180min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	12
9H-fluoren-9-one; anthracene-9,10-dione; Benzo[a]anthracene-7,12-dione; Benzanthrone; 9,10-dihydrobenzo[a]pyren-7(8H)-one	0.91 - 4.41 (w.w.)	0.003 - 0.207	-	Youtiao (fried bread)	LLE – SPE **Solvent:** n-hexane (~ 1 L/sample) and acetonitrile:acetone 3:2 (~ 36 ml/sample); **extraction time:** 243 min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	13

9H-fluoren-9-one (DF: 100%); anthracene-9,10-dione (DF: 100%); benzo[a]anthracene-7,12-dione (DF: 100%); benzanthrone (DF: 100%); 9,10-dihydrobenzo[a]pyren-7(8h)-one (DF: 100%)	Soybean oil: 0.54 – 9.42 (w.w.) Shortening oil: 0.57 – 3.56 (w.w.)	0.003 - 0.207	-	Youtiao (fried bread) (2)	LLE – SPE **Solvent:** n-hexane (~ 1 L/sample) and acetonitrile:acetone 3:2 (~ 36 ml/sample); **extraction time:** 243 min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	14
9H-fluoren-9-one; anthracene-9,10-dione; benzo[a]anthracene-7,12-dione; benzanthrone; 9,10-dihydrobenzo[a]pyren-7(8h)-one		0.003 - 0.207	-	Fried peanuts (2)	LLE – SPE **Solvent:** n-hexane (~ 1 L/sample) and acetonitrile:acetone 3:2 (10 ml/sample); **extraction time:** 190 min; **clean up** (C18 SPE + Florisil SPE); **evaporation/reconstitution steps:** yes	GC-MS	15
Anthracene-9,10-dione; 2-Methyl-anthraquinone; **9H-fluoren-9-one; naphtacene-5,12-dione**	n.d. - 0.4 (∝g/L)	0.031 - 0.048 (∝g/L)	0.102 - 0.16 (∝g/L)	Coffee brew (27)	DI – CF – SPME **Solvent:** acetontrile (0.15 mL/sample); **extraction time:** 47 min; **clean up:** no **evaporation/reconstitution steps:** no	GC-MS	16
Anthracene-9,10-dione; naphtacene-5,12-dione; 2-Methyl-anthraquinone; **9H-fluoren-9-one (DF: 7.7%)**	n.d. – 3.75 (∝g/L)	0.003 – 0.128 (∝g/L)	0.011 – 0.427 (∝g/L)	Beers (26)	CF - SPME **Solvent:** Ethyl acetate (0.10 mL/sample); **extraction time:** 47 min; **clean up:** no **evaporation/reconstitution steps:** no	GC-MS	17

[a]*Analytes detected in samples are shown in bold with detection frequency in brackets (when given). PLE: pressurized liquid extraction; MARS: Microwave-accelerated reaction system; LLE: liquid-liquid extraction; SPE: solid phase extraction; DI-CF-SPME: direct immersion cold fiber solid phase microextraction, d.w.: dry weight, w.w.: wet weight. References:* ***(1).*** *De Witte, B., Walgraeve, C., Demeestere, K. and Van Langenhove, H. 2019. Oxygenated polycyclic aromatic hydrocarbons in mussels: analytical method development and occurrence in the Belgian coastal zone. Environ. Sci. Pollut. Res. 26, 9065–9078. Doi: 10.1007/s11356-019-04259-2.* ***(2)*** *Layshock, J.A., Wilson, G. and Anderson, K. A. 2010. Ketone and quinone-substituted polycyclic aromatic hydrocarbons in mussel tissue, sediment, urban dust and diesel particulate matrices. Environ. Toxic. Chem. 29, 2450-2460. Doi: 10.1002/etc.301.* ***(3)*** *Bandowe, B.A., Bigalke, M., Boamah, L., Nyarko, E., Saalia, F.K. and Wilcke, W. 2014. Polycyclic aromatic compounds (PAHs and oxygenated PAHs) and trace metals in fish species from Ghana (West Africa): bioaccumulation and health risk assessment. Environ. Int. 65, 135-46. Doi: 10.1016/j.envint.2013.12.018.* ***(4)*** *Ranjbar Jafarabadi, A., Riyahi Bakhtiari, A., Yaghoobi, Z., Kong Yap, C., Maisano, M. and Capello, T. 2019. Distributions and compositional patterns of Polycyclic Aromatic Hydrocarbons (PAHs) and their derivatives in three edible fishes from Kharg coral Island, Persian Gulf, Iran. Chemosphere, 215, 835-845. Doi: 10.1016/j.chemosphere.2018.10.092.* ***(5)*** *Chen, Y., Shen, G., Su, S., Shen, H., Huang, Y., Li, T., Li, W., Zhang, Y., Lu, Y., Chen, H., Yang, C., Lin, N., Zhu, Y., Fu, X., Liu, W., Wang, X. and Tao, S. 2014. Contamination and distribution of parent, nitrated, and oxygenated polycyclic aromatic hydrocarbons in smoked meat. Environ. Sci. Pollut. Res. Int. 19, 11521-11530. Doi: 10.1007/s11356-014-3129-8.* ***(6)*** *Zastrow, L., Speer, K., Schwind, K. H. and Jira, W. 2021. A sensitive GC-HRMS method for the simultaneous determination of parent and oxygenated polycyclic aromatic hydrocarbons in barbecued meat and meat substitutes. Food Chem. 365, 130625. Doi: 10.1016/j.foodchem.2021.130625.* ***(7)*** *Zastrow, L., Schwind, K. H., Schwagele, F. and Speer, K. (2019).*

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Extraction of oxy-PAHs from food is mainly carried out with pressurized liquids (De Witte et al., 2019; Bandowe et al., 2014), microwaves (Chen et al., 2014) or conventional extraction with different organic solvents (Teng, Wu & Gong, 2019; Hua, Zhao, Wu & Li, 2016; Gong, Wu & Wu, 2019; Gong, Zhao & Wu, 2018; Li, Wu, Zeng, Wang & Yu, 2016; Zhao, Wu, Gong, Li & Zhuang, 2017; Zhao, Gong & Wu, 2018) usually followed by clean-up with solid phase extraction and evaporation/concentration steps. Since these methods consume high volumes of toxic organic solvents and they are based on multiple time-

consuming and costly steps, new alternatives have been proposed, like immersion fiber microextraction (Dos Santos, Vidotti Leal, de Lourdes Cardeal & Menezes, 2019), being this methodology limited to liquid samples. In addition, it is usual to use gas chromatography-mass spectrometry (GC-MS) for oxy-PAHs determination, but due to the fact that some of these compounds form artifacts (such as the formation of 9H-fluoren-9-one after CO elimination from phenanthrene-9,10-dione) and that some of them are thermolabile, liquid chromatography (LC)-MS is recommended to overcome these issues (Sklorz et al., 2007; Sklorz, Schnelle-Kreis, Liu, Orasche & Zimmermann, 2007; Walgraeve, Demeestere, Dewulf, Zimmermann & Van Langenhove, 2010; Liu et al., 2005).

The search for greener solvents and miniaturized extraction formats that are in line with green chemistry principles is an active field in analytical chemistry. Supramolecular solvents (SUPRASs) meet many of the criteria set for green solvents (Gu & Jérôme, 2014) and they are particularly suitable for application in miniaturized extraction formats. SUPRASs are nanostructured liquids spontaneously formed by sequential self-assembly and coacervation of colloidal suspensions of amphiphiles under the action of a coacervating agent (Ballesteros-Gómez, Sicilia & Rubio, 2010). A schematic representation of SUPRAS formation is shown in Figure S1 (Supporting Information). SUPRASs present several advantageous characteristics in extraction processes: (a) different polarity microenvironments and mixed-mode interactions, (b) multiple binding sites, (c) large surface area, (d) restricted access properties for the exclusion of macromolecular matrix components, (e) simple and energy-less preparation, and (f) low toxicity when environmental-friendly amphiphiles, solvents and additives are employed (Ballesteros-Gómez et al., 2010; Ballesteros-Gómez & Rubio, 2012).

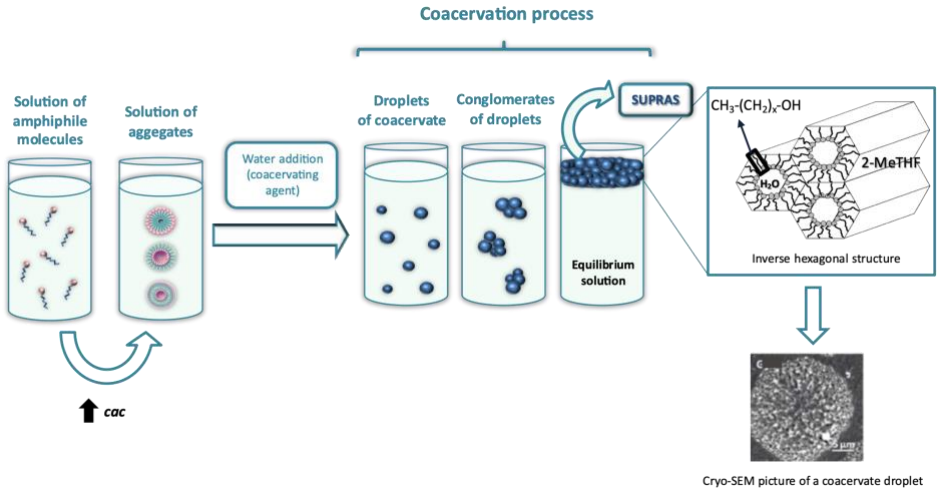


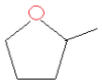
Figure S1. *Scheme of SUPRAS preparation.*

SUPRASs have been successfully employed for the extraction of a variety of organic contaminants from environmental, biological and food samples (Ballesteros-Gómez et al., 2010), including PAHs (Ballesteros-Gómez, Rubio & Pérez-Bendito, 2007; Ballesteros-Gómez, Rubio & Pérez-Bendito, 2008; Falsafi, Raofie & Ariya, 2020). SUPRASs can be applied in microextraction formats (SUPRASs volumes are usually in the range 0.1-0.5 mL) using simple processes, which mostly consist in a single extraction/clean-up step carried out by simple agitation at room temperature without the need of further evaporation/reconstitution steps. However, many of the SUPRASs used so far have been produced from toxic organic co-solvents and amphiphiles from petrochemical origin (such as tetrahydrofuran or non-ionic surfactants), which has hindered their sustainability. In this sense, alternatives have been proposed, such as the use of carboxylic acids (Ballesteros-Gómez et al., 2007; Ballesteros-Gómez et al., 2008), fatty alcohols (Ballesteros-Gómez & Rubio, 2012) and rhamnolipids (Romera-García, Ballesteros-Gómez & Rubio, 2020). These amphiphiles are sustainable, non-toxic and can be obtained from renewable sources. SUPRASs made up of reverse micelles of fatty alcohols in THF:water mixtures have been widely used in the extraction of organic contaminants (Ballesteros-Gómez et al., 2010). The low dielectric constant

of THF resulted in wide SUPRASs formation diagrams (Ballesteros-Gómez & Rubio, 2012) and in highly hydrophobic microenvironments at the THF-solvated hydrocarbon layers of the reverse aggregates that were suitable for the extraction of medium to highly apolar compounds. (Ballesteros-Gómez et al., 2010; Ballesteros-Gómez & Rubio, 2012).

In this study, SUPRASs of inverse aggregates made up of short/medium chain length alcohols were produced by replacing THF by its more sustainable homologous, methyl-THF (2-MeTHF). The use of organic solvents that can be produced from renewable sources provide better sustainability (Engiezcu et al., 2020; Mudge, 2005). The formation, composition and microstructure of SUPRASs of reverse aggregates of fatty alcohols in mixtures of 2-MeTHF:water are here described for the first time. The applicability of these new SUPRASs is tested for the extraction of four oxy-PAHs from complex samples (food based on meat and fish) prior to their determination by liquid chromatography coupled to high resolution mass spectrometry (LC-APCI-QTOF). Based on the similar physico-chemical characteristics and solubility properties of both solvents (dielectric constant, Hildebrand solubility parameter, see Table S2) SUPRASs of similar structure and extraction capabilities but greener were expected. The sustainability of 2-MeTHF is supported by life-cycle assessment data. As shown in Table S2, 2-MeTHF shows better scores than THF for most of the environmental indicators. For the optimization of sample preparation, several variables were tested (amphiphile chain length and 2-MeTHF percentage) and their influence in both extraction efficiency and matrix effects were investigated. Due to the scarce literature on the presence of oxy-PAHs in food and in order to provide information about contamination levels in food items from Spanish supermarkets, the optimized method was applied to the extraction of 19 samples of processed meat, seafood and fish samples. Target oxy-PAHs were naphtacene-5,12-dione, 6H-benzo(cd)pyren-6-one and 11H-benzo(b)fluoren-11-one, all of them proposed as priority compounds given their toxicity (Clergé et al., 2019) and 9H-fluoren-9-one, an ubiquitous and frequently analyzed oxy-PAH.

Table S2. Physico-chemical properties and life-cycle assessment data of tetrahydrofuran (THF) and methyl-tetrahydrofuran (2-MeTHF)

	THF	2-MeTHF
Structure		
CAS	109-99-9	96-47-9
[a]Physico-chemical properties		
Boiling point	66°C	80°C
Melting point	-108.5°C	-136°C
Density (20°C)	0.89g/cm^3	0.85g/cm^3
Vapor pressure (20°C)	162.22mmHg	102mmHg
Relative permittivity	7.4	6.97
Dipole moment	1.75D	1.38D
Hildebrand solubility parameter	10.01MPa$^{1/2}$	16.9MPa$^{1/2}$
Dielectric constant	7.58	6.97
Water solubility	Miscible (25°C)	14g/100g water (20°C)
Viscosity (cP)	[a]0.53 (20°C)	[a]0.46 (25°C)
Life-cycle assesment data		
CO_2 emissions (Kg)	[b]5.46	[b]0.15
Water emissions (Kg)	[c]0.0023	[b]0.0273
Air emissions (Kg)	[c]5.52	[b]0.162
Soil emission (Kg)	[c]0.0023	[b]0.0019
Total cumulative energy demand (MJ)	[c]128	[b]-20
Total raw material used (including water) (Kg)	[c]713	[b]121

2. Experimental section

2.1. Chemicals and reagents

The organic solvents methanol (MeOH) and acetonitrile (ACN) were supplied by Fisher Scientific (Madrid, Spain) and methyl-tetrahydrofuran (2-MeTHF) was supplied by Sigma-Aldrich (St. Louis, MO, USA). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain).

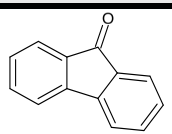
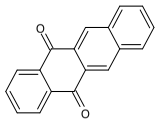
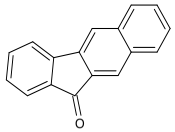
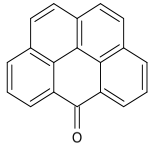
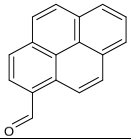
The amphiphile 1-hexanol was acquired from Merck (Darmstadt, Germany), while 1-octanol and 1-decanol were provided by Sigma-Aldrich (St. Louis, MO, USA). The target compounds were naphtacene-5,12-dione

(5,12-Napht, CAS 1090-13-7, purity of 97%), 11H-benzo[b]fluoren-11-one a [11-B(b)Fluo, CAS 3074-03-1, purity of 95%] and 9H-fluoren-9-one (9-Fluo, CAS 486-25-9, purity of 98%), obtained from Sigma-Aldrich (St. Louis, MO, USA), while 6H-Benzo[cd]pyren-6-one [6-B(cd)Pyr, CAS 3074-00-8, purity of 97%] was supplied by BCR (Community Bureau of Reference, European Commission) (BCR-339). The internal standard (IS) 1-pyrenecarboxaldehyde (CAS 3029-19-4, purity of 99%) was acquired from Sigma-Aldrich (St. Louis, MO, USA). Table S3 provides detailed information about the target compounds (chemical structure, exact mass and log P). Stock solutions of individual oxy-PAHs and IS were prepared in ACN (100 mg·L^{-1}) and stored at 4ºC. Intermediate and working solutions were prepared by appropriate dilution in ACN and stored as well at 4ºC.

2.2. Apparatus

The determination of oxy-PAHs was carried out using a LC system (Bruker ELUTE HPLC) with a RESTECK C18 column (100 mm x 3.0 mm, 3µm particle size) preceded by a precolumn from Phenomenex (KJ 0-4282 Security Guard Cartridge Kit). The LC system was coupled to a high resolution mass spectrometer (Bruker TimsTOF, Q-TOF) equipped with an atmospheric pressure chemical ionization source (APCI) operating in positive mode. Optimized source parameters were: end plate offset, 500V; capillary voltage, 2500V; corona voltage, 3000 nA; nebulizer gas pressure, 2.5 Bar; dry gas, 3 L/min; dry temperature, 200 ºC; vaporizer temperature, 350ºC. The mobile phase was made up of water (A) and MeOH (B) at a flow rate of 0.2 mL·min^{-1}. The gradient started with 60% of B during 1 min, increasing until 99% in the next 9 min, and maintaining isocratic conditions during 5 min, followed by 7 min for reconditioning the column with initial conditions. Acquisition was developed in broadband collision-induced dissociation (bbCID) mode (collision energy 35 eV, 3 Hz, *focus on, profile spectra*). Data processing was carried out with Data Analyst program (Bruker Daltonics).

Table S3. Target oxy-PAHs and internal standard (IS)

Analyte	CAS	Formula (exact masss)	Structure	[a,b]Log P	Exact mass (Da)	Quantifier ion	Qualifier ions
9H-fluoren-9-one (9-Fluo)	486-25-9	$C_{13}H_8O$		[a]3.6	180.0575	**$[M+H]^+$**, $C_{13}H_9O$ (181.0648)	$[M+H-CO]^+$ $C_{12}H_9$ (153.0704) $[M-CO]^+$ $C_{12}H_8$ (152.0626)
Naphtacene-5,12-dione (5,12-Napht)	1090-13-7	$C_{18}H_{10}O_2$		[b]4.6	258.0680	**$[M+H]^+$**, $C_{18}H_{11}O_2$ (259.0754)	$[M+H-CO]^+$ $C_{17}H_{11}O$ (231.0810) $[M+H-C_2O_2]^+$ $C_{16}H_{11}$ (203.0861) $[M-C_2O_2]^+$ $C_{16}H_{10}$ (202.0783)
11H-benzo[b]fluoren-11-one [11-B(b)Fluo]	3074-03-1	$C_{17}H_{10}O$		[b]4.8	230.0732	**$[M+H]^+$**, $C_{17}H_{11}O$ (231.0804)	$[M+H-CO]^+$ $C_{16}H_{11}$ (203.0861) $[M-CO]^+$ $C_{16}H_{10}$ (202.0783)
6H-Benzo[cd]pyren-6-one [6-B(cd)Pyr]	3074-00-8	$C_{19}H_{10}O$		[b]5.2	254.0732	**$[M+H]^+$**, $C_{19}H_{11}O$ (255.0804)	$[M-CO]^+$ $C_{18}H_{10}$ (226.0783)
1- Pyrenecarboxaldehyde (IS)	3029-19-4	$C_{17}H_{10}O$		[a]4.2	230.0726		

Source Pubchem, [a]Experimental value, [b]Calculated value.

Apparatus used in sample preparation were a vortex-shaker REAX Top (Heidolph, Schwabach, Germany) and a Mixtasel Select Centrifuge (Barcelona, Spain). The water content in SUPRASs was measured with a Karl Fischer Coulombimetric valorator (KF 831 model, Metrohm, Hisao, Switzerland). An optical microscope Leica model DME instrument (Wetzlar, Germany) equipped with an automatic photocamera was used to study the structure of coacervate droplets of SUPRASs, whose sizes were measured with the program ImageJ (NIH, US), and a scanning electron microscopy (SEM) Zeiss EVO LS15 (Zeiss Microscopy) was employed to study the morphology of the SUPRASs aggregates. The statistical package Statgraphics Centurion XV.II was used to design the SUPRASs volume prediction model.

2.3. SUPRASs characterization

SUPRASs were characterized in terms of composition, volume and structure. They were made up from ternary solutions of amphiphile, 2-MeTHF and water, the later acting as coacervating agent (poor solvent for the amphiphile). Mixtures were vortex-stirred for 1 min and centrifuged for 5 min at 2,500 rpm for phase separation after which SUPRAS stood at the top and the aqueous equilibrium solution (EqS) at the bottom, containing residual amounts of amphiphile and of organic solvent.

The water content in SUPRASs was measured by Karl Fischer reaction weighing an aliquot of SUPRAS (50 µL) followed by MeOH dilution (1:20, v/v), prior to injection (200 µL aliquot) in the titration cell. The amphiphile content was calculated after both water and 2-MeTHF evaporation. Finally, 2-MeTHF content was calculated as the difference between the total content (100%) and the percentages of the previously measured components. All experiments were made in triplicate.

The generated volume of SUPRAS under different formation conditions was calculated by measuring its height in a cylindrical tube

with a digital calliper and using the equation $V=\pi \cdot r^2 \cdot h$. Non-linear regression was used to fit a model in order to predict the formed SUPRAS volume from the different ternary mixtures.

Regarding SUPRASs structure, the presence of coacervate droplets in the SUPRAS phase was investigated by optical microscopy. Due to the fact that organic solvent evaporates easily under light microscopy, micrographs had to be taken immediately after placing SUPRAS on microscope slides.

The morphology of the SUPRASs aggregates was investigated with SEM. A SUPRAS aliquot of ~10 μL was fixed with glutaraldehyde and embeddedness with a 6% aqueous agarose solution, followed by three times washing with sodium cacodylate. Then, it was stained with OsO_4 (1%) for contrast enhancement. After that, it was dehydrated with a graded series of acetone (30, 50, 70, 80, 90, 100 %) and dried using the critical point drying. Finally, samples were coated with gold and observed under SEM. The accelerating voltage was set at 10 kV.

2.4. Optimization of SUPRAS extraction of oxy-PAHs from food samples

SUPRAS was formed from 5% v/v of 1-hexanol, 1-octanol and 1-decanol in different mixtures of 2-MeTHF:water v/v in 50 mL polypropylene centrifuge tubes as explained in section 2.3. The resulting SUPRAS and EqS were stored in closed polypropylene centrifuge tubes at 4°C until use. In order to optimize sample extraction, samples of processed chicken and cooked mussels were acquired from a local supermarket in Córdoba (Andalusia, Spain). Samples were homogenized with a commercial blender. Wet aliquots of 200 mg, fortified with the target compounds and the IS (20 $ng \cdot g^{-1}$ each), were added in 2 mL microtubes, followed by the addition of 300 μL of EqS (dispersion phase to facilitate the mass transfer process) and 200 μL of SUPRAS (extraction phase).

Mixtures were vortex stirred for 10 min and centrifuged during 20 min at 10,000 rpm. The ratio 1:1.5:1 sample:EqS:SUPRAS (g:mL:mL) was initially set to ensure good sample dispersion during stirring and to obtain an abundant top SUPRAS phase after centrifugation. This allowed an efficient mass transfer process in a short stirring time and the collection of ~200 µL aliquots to be transferred to LC vials with inserts. SUPRAS composition was optimized in terms of different amphiphiles (1-hexanol, 1-octanol, 1-decanol) and different preparation percentages of 2-MeTHF (2.5-10% v/v). These variables were assessed on the basis of both extraction efficiency and matrix effects. Experiments were made in triplicate. One-way ANOVA and post-hoc Tukey tests were used to investigate significant differences between results.

2.5. Analysis of processed meat, seafood and fish samples

SUPRASs were made up from solutions of 5% v/v of 1-hexanol, 5% of 2-MeTHF and 90% v/v of water for the processing of meat samples and from solutions of 5% v/v of 1-hexanol, 7.5% of 2-MeTHF and 87.5% v/v of water for fish and seafood sample preparation. Calibration curves were prepared in SUPRAS to ensure the same injection medium in standards and in samples. Sample extraction was carried out with 200 mg wet sample, 200 µL of SUPRAS and 300 µL of EqS. Samples of processed meat (7), fish (5) and seafood (7) were acquired from local supermarkets in Córdoba (Andalusia, Spain) between January and March of 2021.

2.6. Method validation

A preliminary validation of the analytical method was carried out using the optimized selected conditions (specified in section 2.5.). Identification of compounds was done on the basis of the following criteria:

mass error below 5 ppm for quantifier and qualifier ions, isotopic pattern fit (mSigma ≤100) for quantifier ion and retention time match (±0.1 min).

The linearity of the standard solutions was evaluated in the range 0.05 - 50 $\mu g \cdot L^{-1}$ (n=16). Sensitivity was calculated in terms of limits of detection (LODs) and limits of quantification (LOQs), which were estimated at a signal-to-noise ratio of 3 and 10 of the quantifier ion (with the detection of at least one qualifier ion), respectively. Accuracy was expressed as recovery and intra-day and inter-day precision as relative standard deviation in fortified samples (triplicates) of processed chicken and mussel at different concentration levels (5, 10, 30 and 50 $ng \cdot g^{-1}$, and 20 $ng \cdot g^{-1}$ of IS).

3. Results and discussion

3.1. SUPRASs characterization

3.1.1. SUPRASs formation and chemical composition

Formation of the SUPRASs was tried by dissolving the amphiphile (1-hexanol, 1-octanol or 1-decanol) in 2-MeTHF and then adding water as the coacervating agent. The maximum percentage of 2-MeTHF used for the preparation of the SUPRASs was determined by its solubility in water (~ 14 % w/w at 20°C). It was checked that SUPRASs were formed at the following proportions of the ternary mixture: 2.5-15% v/v of amphiphile, 2.5-12.5% v/v of 2-MeTHF and 72.5-95% v/v of water.

As it is shown in Table 1, the concentration of amphiphile in the SUPRASs was very high (63-95% w/w, Table 1), which result in multiple binding sites for the extraction of analytes. Mixed-mode interactions are expected, namely dispersion forces and methanetriyl-pi hydrogen bonding (CH-π HB) (Algar, Sicilia & Rubio, 2022) at the nonpolar domains of SUPRASs, and dipole-dipole and hydrogen bonding interactions at the polar microenvironments given by the alcohol groups and the water in the SUPRASs.

Table 1. SUPRASs composition prepared with 5 % v/v 1-hexanol, 1-octanol or 1-decanol and several 2-MeTHF percentages (%, v/v)

%, v/v 2-MeTHF for SUPRAS formation	% Amphiphile (w/w)	% Water (w/w)	% 2-MeTHF (w/w)
	1-hexanol SUPRAS		
2.5	87.4 ± 0.1	6.5 ± 0.3	6.1 ± 0.4
5	82.0 ± 0.4	8.0 ± 0.2	10.0 ± 0.6
7.5	75.71 ± 0.04	9.1 ± 0.2	15.2 ± 0.2
10	69.22 ± 0.02	9.7 ± 0.1	21.1 ± 0.2
12.5	63.19 ± 0.06	10.29 ± 0.02	26.52 ± 0.04
	1-octanol SUPRAS		
2.5	91.6 ± 0.9	4.8 ± 0.1	3.6 ± 1.0
5	88.3 ± 0.3	4.9 ± 0.2	6.9 ± 0.5
7.5	82.9 ± 0.5	5.2 ± 0.4	11.93 ± 0.06
10	77.5 ± 0.6	5.3 ± 0.3	17.2 ± 0.8
12.5	72.2 ± 0.3	6.07 ±0.02	21.8 ± 0.3
	1-decanol SUPRAS		
2.5	95.1 ± 0.3	3.39 ± 0.07	1.5 ± 0.4
5	90.9 ± 0.4	3.6 ± 0.2	5.5 ± 0.2
7.5	85.4 ± 0.6	3.8 ± 0.3	10.8 ± 0.3
10	81.9 ± 0.1	4.1 ± 0.4	13.9 ± 0.4
12.5	78.58 ± 0.07	4.4 ± 0.3	17.1 ± 0.2

3.1.2. SUPRASs volume

The volume of SUPRAS generated in the ternary mixture increased linearly with both the percentage of amphiphile and 2-MeTHF, regardless of the alcohol chain length (Tables S4 and S5). To predict the SUPRAS volume as a function of amphiphile and 2-MeTHF the following equations were obtained by nonlinear regression:

$$V_{SUPRAS} = [(0.2526 * Z + 18.9565) * X + (7.7008 * Z - 61.5847)] \quad (1)$$

$$V_{SUPRAS} = [(0.45739 * Z + 16.3632) * X + (5.0183 * Z - 38.3921)] \quad (2)$$

$$V_{SUPRAS} = [(0.33027 * Z + 16.9675) * X + (6.1762 * Z - 44.4891)] \quad (3)$$

for 1-hexanol (1), 1-octanol (2) and 1-decanol (3), respectively.

Table S4. Equations and coefficients of determination of linear regression lines corresponding to plots of SUPRAS volume as a function of amphiphile percentage (2.5-15%, v/v) at different organic solvent percentages

	Synthesis condition (2-MeTHF, %, v/v)	Equation	Coefficient of determination
1-hexanol	2.5	y = 200.2x – 432.48	0.999
	5	y = 196.93x - 213.01	0.999
	7.5	y = 206.72x - 28.70	0.999
	10	y = 216.92x +118.3	0.999
	12	y = 221.78x + 364.47	0.995
1-octanol	2.5	y = 168.84x – 215.54	0.995
	5	y = 191.21x – 174.85	0.998
	7.5	y = 202.44x – 23.83	0.997
	10	y = 211.16x + 104.47	0.995
	12	y = 216.09x + 269.4	0.994
1-decanol	2.5	y = 174.57x – 252.15	0.995
	5	y = 188.05x – 177.58	0.999
	7.5	y = 195.49x + 18.56	0.992
	10	y = 208.49x + 143.33	0.994
	12	y = 205.69x + 356.33	0.996

Table S5. Equations and coefficients of determination of linear regression lines corresponding to plots of SUPRAS volume as a function of organic solvent percentage (2.5-12.5%, v/v) at different amphiphile percentages

	Synthesis condition (amphiphile, % v/v)	Equation	Coefficient of determination
1-hexanol	2.5	y = 78.94x – 138.04	0.9991
	5	y = 86.73x + 373.99	0.995
	8	y = 94.09x + 921.44	0.992
	12	y =111.77x + 1608.3	0.994
	15	y =107.67x + 2277.6	0.993
1-octanol	2.5	y = 54.63x + 15.86	0.990
	5	y = 83.73x + 402.44	0.993
	8	y = 112.91x + 844.83	0.994
	12	y = 102.38x + 1637.6	0.991
	15	y = 136.62x + 1930.5	0.992
1-decanol	2.5	y = 56.27x + 67.24	0.983
	5	y = 91.17x + 302.46	0.997
	8	y = 107.71x + 880.61	0.996
	12	y = 98.70x + 1637.2	0.990
	15	y = 109.75x + 2065.1	0.993

Although the dependence between the SUPRAS volume and the percentage of organic solvent in the preparation mixture has been described before as exponential (Ballesteros-Gómez, Sicilia & Rubio, 2010), the limited range of 2-MeTHF (2.5-12.5% v/v) in comparison with that of THF (from 2.5 up to ~80-90% v/v) for SUPRAS formation resulted in a linear dependence.

The dependent variable (V_{SUPRAS}) is the SUPRAS volume (μL) produced per mL of ternary mixture, being the independent variables X and Z, the amphiphile and the 2-MeTHF percentages (v/v), respectively. Equations were valid within the ranges 2.5-15% (v/v) of amphiphile and 2.5-12.5% (v/v) of 2-MeTHF with coefficients of determination of 0.998, 0.995 and 0.995 for 1-hexanol, 1-octanol and 1-decanol, respectively (see Figure S2).

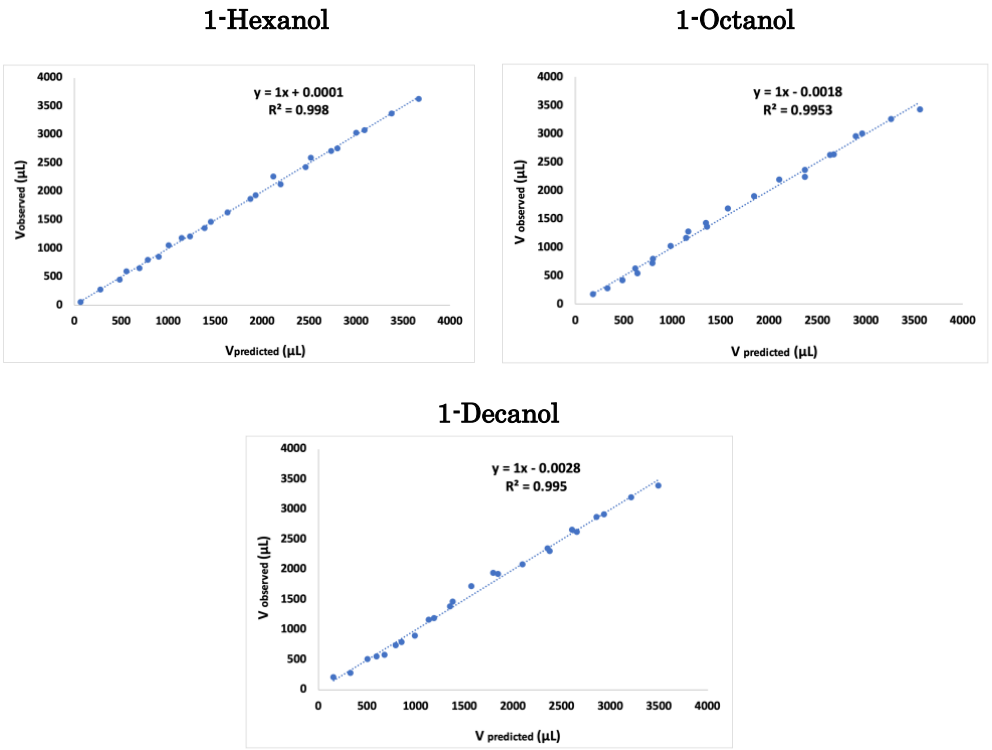


Figure S2. *Agreement between the measured volumes of SUPRAS (μL) and those calculated using the proposed equation. Synthesis final volume: 15 mL.*

3.1.3. Characterization of SUPRASs structure

Figures 1A and 1B, respectively revealed that SUPRASs were not continuous liquids and that they were formed by a cluster of hexagonal droplets with sizes in the range of 2 – 5 μm (mean value 3.8 μm) and 3 - 6 μm (mean value 4.3 μm) for 5% and 7.5% of 2-MeTHF, respectively.

The morphology of SUPRASs was also investigated by scanning electron microscopy (SEM, Figures 1C and 1D). Hexagonal structures could be clearly distinguished where water pools or channels could be allocated. So, on the whole, replacement of THF by the greener 2-MeTHF produced SUPRASs of similar chemical composition and morphology but their production was more sustainable since all the ingredients can be obtained from biomass and they can be considered as bioSUPRASs.

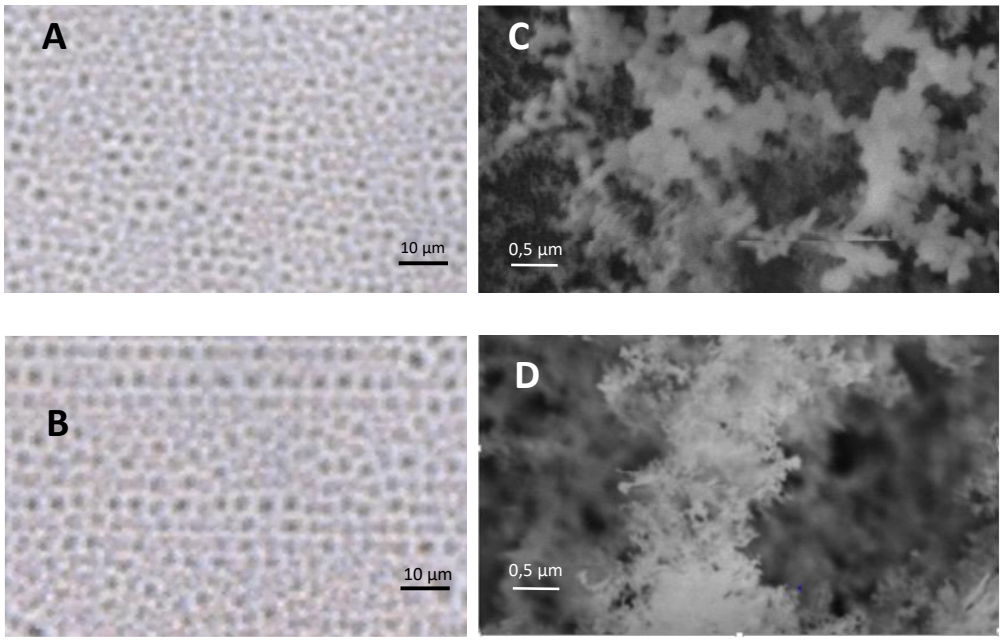


Figure 1. *Optical micrographs of SUPRASs prepared with 5% of 1-hexanol and 5% (A) and 7.5% (B) of 2-MeTHF. SEM micrographs of SUPRASs synthetized by 5% of 1-hexanol and 5% (C) and 7.5% (D) of 2-MeTHF.*

3.2. Optimization of SUPRASs extraction

3.2.1. Influence of the amphiphile chain length

Optimization of SUPRASs extraction of oxy-PAHs from food samples was carried out according to the procedures specified in section 2.4. First, the influence on the extraction process of SUPRASs made up of fatty alcohols of different chain length (C_6, C_8, C_{10}) was investigated. For this aim, SUPRASs were prepared with these three amphiphiles (5% v/v), 2-MeTHF (10% v/v) and water (85 % v/v). Figure 2 shows the results. Total recoveries were estimated by spiking the samples with analytes and IS before extraction. Matrix effects (signal suppression or enhancement) were calculated by spiking SUPRAS extracts after the extraction process. The IS was selected on basis of bibliography [De Witte et al., 2019]. Both absolute ($A_{analyte}$) and relative ($A' = A_{analyte}/A_{IS}$) areas in SUPRAS extracts were compared to those measured in standards prepared in SUPRAS at the same concentration level (A or $A'_{\text{analyte in SUPRAS extract}}/A$ or $A'_{\text{analyte in standard}} *100$).

In absolute terms, matrix effects for SUPRASs made up of different amphiphiles were not be very accused (see figure 2A) and they were slightly lower in mussels samples (94-114%, relative standard deviation (RSD): 10-27%, median RSD: 19%) than in chicken samples (115-146%, RSD: 4-15%, median RSD: 6%). IS correction (figure 2B) slightly improved these values, which were in the intervals of 87-104% (RSD: 5-14%, median RSD: 7%) in mussels and 88-110 % (RSD: 2-10%, median RSD: 5%) in chicken. Significant differences among the different types of SUPRASs (after IS correction) were only found for 11-B(b)fluo in chicken, being values 93±7, 88±3 and 110±4 for SUPRASs of 1-hexanol, 1-octanol y 1-decanol, respectively.

Total absolute recoveries, which represent all the process variability (including matrix effects and extraction efficiency, among others), varied between 64 and 125% (RSD: 5-19%, median RSD: 16%) in mussels and between 72 and 117% (RSD: 6-11%, median RSD: 9%) in

chicken. Relative values (or apparent recoveries with IS correction) varied in the ranges of 60-113% (RSD: 6-20%, median RSD: 9%) in mussels and of 64-120% (RSD 1-14%, median RSD: 7%) in chicken.

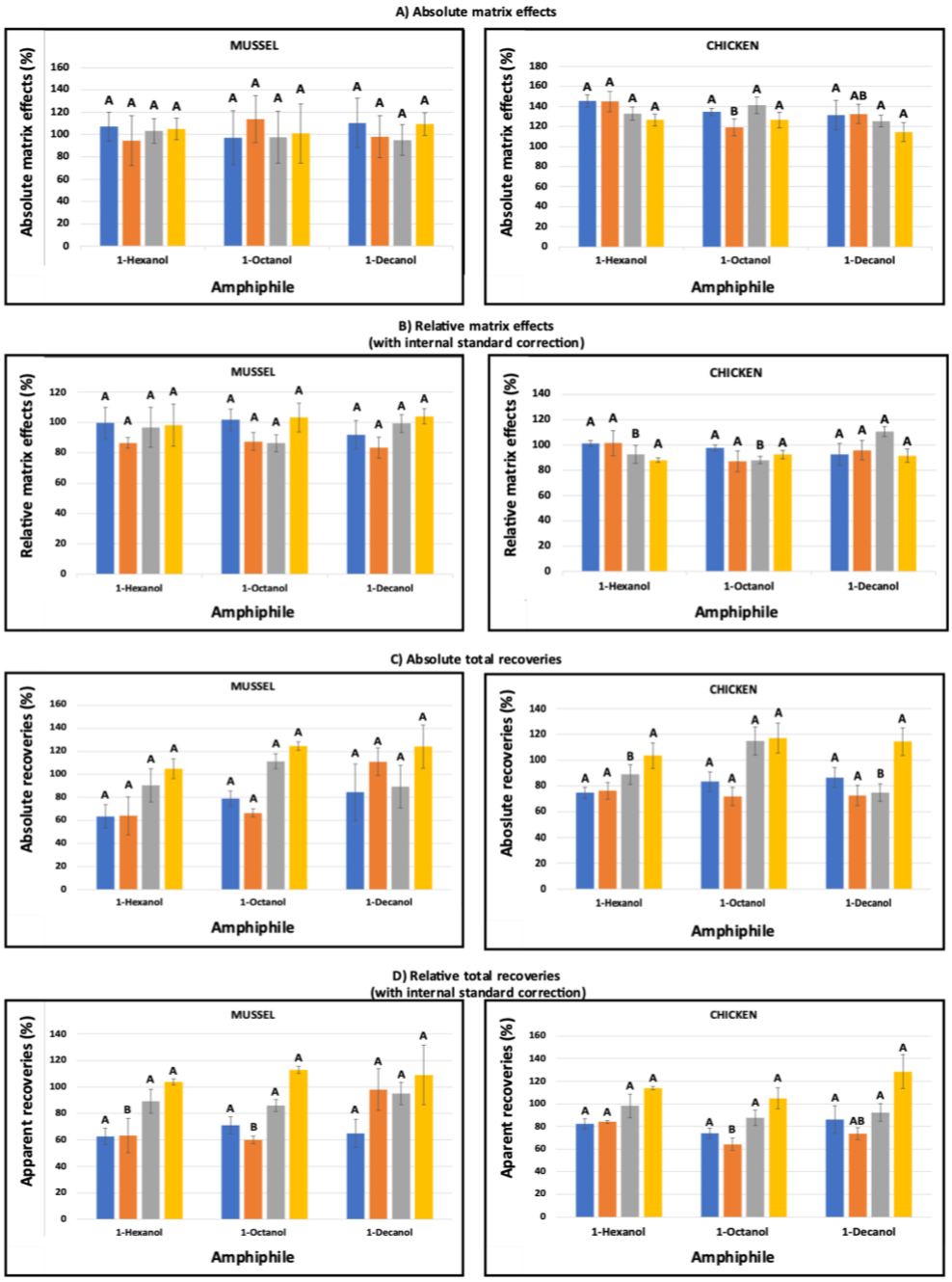


***Figure 2**. Matrix effects and total recoveries in absolute and relative values (corrected with IS) in SUPRASs with different alcohol chain length. Experiments done in triplicate. Different letters show significant differences between results (ANOVA/Tukey test, significance level 0.05). Analytes: blue: 5,12-Napht; Orange: 6-B(cd)pyr; gray: 11-B(b)fluo and yellow: 9-Fluo.*

In this case, the IS correction mainly improved the median RSD. Significant differences between SUPRASs appeared only for 6-B(cd)pyr after IS correction. For this oxy-PAH, the recoveries were significantly lower in SUPRAS of 1-octanol in mussels (60±3) and in chicken (64±5) and in SUPRAS of 1-decanol in chicken (73±5). These differences did not appear in the assessment of relative matrix effects so they should be due to the different extraction capabilities of SUPRASs. The highest content in 2-MeTHF of SUPRAS made up of 1-hexanol (see Table 1) could have enhanced the extraction of this more apolar compound. Accordingly, 1-hexanol was selected as optimized for SUPRAS formation, which provided relative total recoveries in the ranges 63-104% for mussels and 82-114% for chicken.

3.2.2. Influence of the 2-MeTHF percentage (% v/v) for SUPRAS formation

Once 1-hexanol was selected as optimized amphiphile for SUPRAS formation, the concentration of 2-MeTHF in the preparation solution was evaluated. Results are shown in Figure 3. Matrix effects were more influenced by the percentage of organic solvent in the preparation in comparison with the chain length of the amphiphile, showing significant differences between the respective SUPRASs, especially in the case of mussels.

When considering both matrix effects and recoveries in absolute terms, the worst results were obtained at the lowest percentages of 2-MeTHF (2.5 and 5% v/v) in mussels. Considering the relative total recoveries or apparent recoveries, the best results were found at 7.5% of 2-MeTHF v/v in mussels with values in the range 94-120% (RSD: 7-11%) and at 5% of 2-MeTHF in chicken with values between 93 and 118% (RSD:2-9%). Although oxy-PAHs are emerging and unregulated compounds, it is worth mentioning that these recoveries are within the recommended

interval by the European guide SANTE/11312/2021 (60-140%; RSD≤20%) for pesticide residues in food and feed.

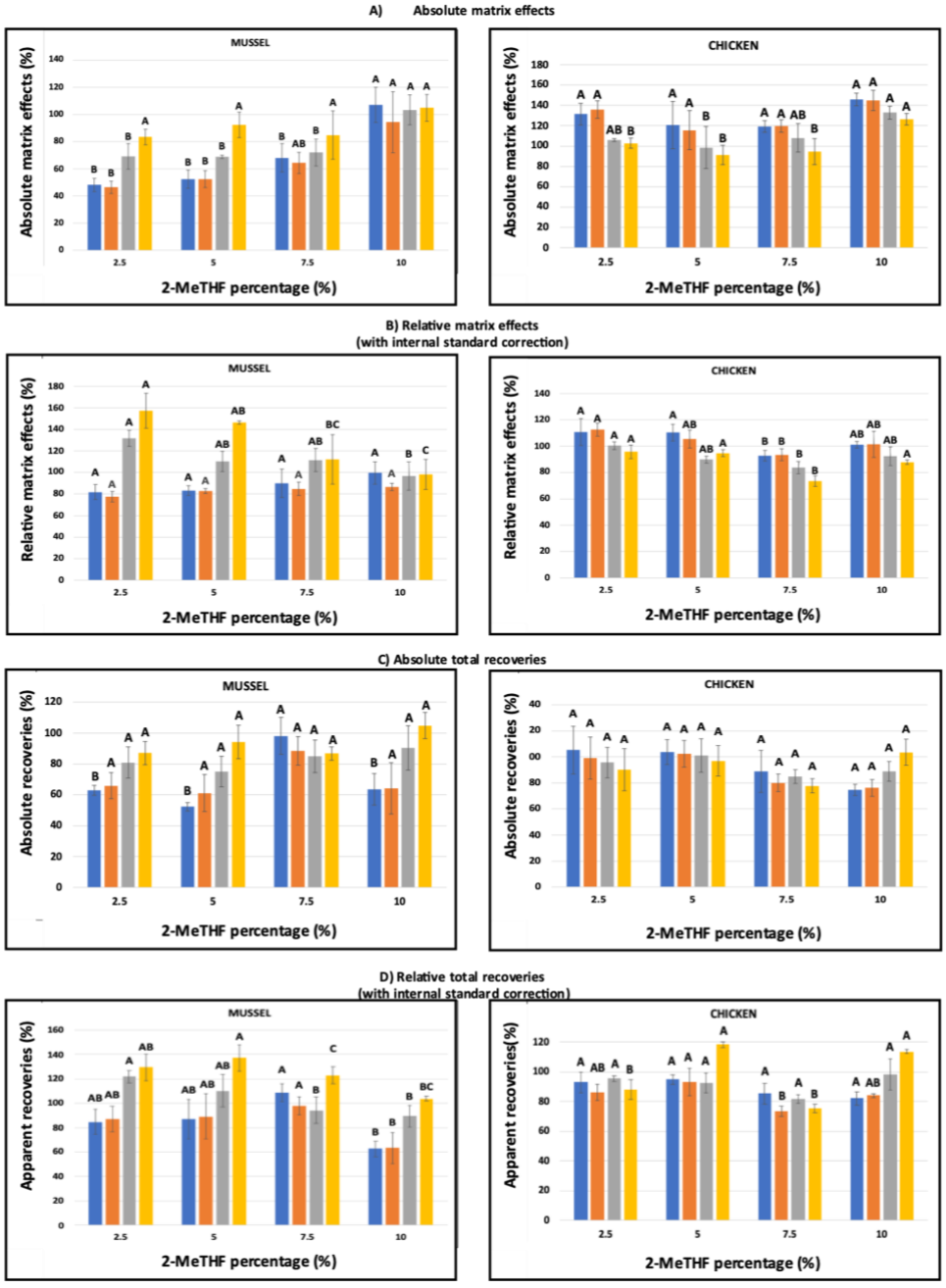


Figure 3. *Matrix effects and total recoveries in absolute and relative values (corrected with IS) in SUPRAS of 1-hexanol and several percentages of 2-MeTHF v/v. Experiments done in triplicate. Different letters show significant differences between results (ANOVA/Tukey test, significance level 0.05). Analytes: blue: 5,12-Napht; Orange: 6-B(cd)pyr; gray: 11-B(b)fluo and yellow: 9-Fluo*

3.3. Method validation

Mussel and chicken samples were fortified at several concentrations (5, 10, 30 and 50 ng·g^{-1}) and accuracy was assessed as apparent recoveries (IS added before extraction). Table 2 shows the results. Recoveries ranged between 70 and 128% and between 70 and 126% for mussels and chicken, respectively. Intra-day precision (n=3) expressed as RSD varied in the ranges 0.06 – 18.5 % and inter-day precision (n=3) varied in the range of 6.9– 17.4% for both mussels and chicken. Values were within the acceptance of SANTE guideline (SANTE/11312/2021).

Table 2. Apparent recoveries of target compounds fortified at four different levels and concentrations of oxyPAHs in blank matrices

		Mussel		Chicken	
	Concentration (ng·g^{-1})	Recovery (n=3)	Blank (ng·g^{-1})	Recovery (n=3)	Blank (ng·g^{-1})
5,12-Napht	5	108 ± 20	n.d.	124 ± 16	n.d.
	10	110 ± 17		70 ± 5	
	30	90 ± 16		114 ± 6	
	50	72 ± 4		95 ± 4	
6-B(cd)pyr	5	88 ± 4	3.5 ± 0.6	108.62 ± 0.06	4.5 ± 0.8
	10	91 ± 7		112 ± 15	
	30	88 ± 16		94 ± 17	
	50	70 ± 10		85 ± 8	
11-B(b)fluo	5	71 ± 1	n.d.	117 ± 22	n.d
	10	85 ± 9		108 ± 6	
	30	102 ± 7		88.3 ± 0.2	
	50	92 ± 4		88 ± 5	
9-Fluo	5	127 ± 4	n.d.	126 ± 15	7.57 ± 0.06
	10	90 ± 14		123 ± 2	
	30	124± 12		115 ± 1	
	50	128± 17		114 ± 1	

Calibration curves for each analyte had good linearity, the percent relative error of the back calculated concentrations at each calibration level lied between ±15 and ±20 at the LOQ and R^2 were in the range 0.9933 – 0.9972 (see Table S6). LODs (0.2 – 1.3 ng·g^{-1}) and LOQ (0.4 – 4 ng·g^{-1}) were in the same order of magnitude than those found in bibliography, e.g LODs in the range 0.08 – 3.57 ng·g^{-1} were reported by De Witte et al. (2019) [De Witte et al. 2019] and similar LOQs (0.3 – 5 ng·g^{-1}) were reported by Bandowe et al. (2014) (see Table S1).

Table S6. Analytical performance of the SUPRAS-based calibration

Analytes	Slope ($L \cdot ug^{-1}$) ± Standard error	R^2	LOD ($ng \cdot g^{-1}$)	LOQ ($ng \cdot g^{-1}$)	RT (min)
5,12-Napht	0.0092 ± 0.0001	0.9972	0.4	1.0	13.0
6-B(cd)pyr	0.0300 ± 0.0007	0.9933	0.2	0.4	13.1
11-B(b)fluo	0.0369 ± 0.0007	0.9949	0.4	1.0	12.1
9-Fluo	0.0181 ± 0.0004	0.9947	1.3	4.0	9.6

3.4. Sample analysis

Processed meat, seafood and fish samples were analyzed with the optimized extraction method. The results obtained are shown in Table 3.

Table 3. Oxy-PAHs concentrations in seafood, fish and meat samples ($ng \cdot g^{-1}$ ww) along with the respective standard deviation

	5,12-Napht	6-B(cd)pyr	11-B(b)Fluo	9-Fluo	Σ Oxy-PAHs ($ng \cdot g^{-1}$)
S1	<LOD	<LOD	<LOD	<LOD	<LOD
S2	8 ± 1	0.6 ± 0.2	<LOD	<LOD	8.6
S3	<LOD	<LOD	<LOD	<LOD	<LOD
S4	<LOD	6.5 ± 0.7	<LOD	<LOD	6.5
S5	<LOD	<LOD	<LOD	<LOD	<LOD
S6	<LOD	<LOD	<LOD	<LOD	<LOD
S7	<LOD	3.5 ± 0.6	<LOD	<LOD	3.5
F1	<LOD	6.1 ± 0.4	<LOD	<LOD	6.1
F2	<LOD	<LOD	<LOD	8 ± 1	8
F3	<LOD	<LOD	<LOD	<LOD	<LOD
F4	<LOD	0.5 ± 0.1	<LOD	4.5 ± 0.9	5
F5	<LOD	<LOD	<LOD	<LOD	<LOD
M1	<LOD	<LOD	<LOD	<LOD	<LOD
M2	<LOD	<LOD	<LOD	<LOD	<LOD
M3	<LOD	<LOD	<LOD	<LOD	<LOD
M4	<LOD	<LOD	<LOD	<LOD	<LOD
M5	<LOD	<LOD	<LOD	<LOD	<LOD
M6	<LOD	<LOD	<LOD	<LOD	<LOD
M7	<LOD	5 ± 1	<LOD	7.6 ± 0.1	12.6

S1: Cooked shrimp; S2: cooked prawns; S3: cooked clams; S4: cooked octopus; S5: cooked squid cubes; S6: cockles. S7: cooked mussel; F1: grated surimi; F2: smoked salmon; F3: ling stick; F4: sausage of tuna and salmon; F5: battered hake balls; M1: baked chicken strips; M2: cooked kebab chicken meat; M3: chicken with serrano ham; M4: roasted chicken breast; M5: roasted chicken with bacon; M6: Frankfurt sausage; M7: chicken kebab.

All the analytes (except 11-B(b)fluo) were found in 7 of 19 samples, mainly in fish and seafood samples. 6-B(cd)pyr was the most detected analyte, in 6 out of 19 samples with values in the interval 0.5 – 6.5 ng g^{-1} ww. It was mainly found in processed seafood samples, being also found together with 9-Fluo in a meat sample (chicken kebab, M7), with concentrations of 5 ± 1 and 7.6 ± 0.1 ng g^{-1} ww, respectively. 9-Fluo was detected in other two fish samples at levels of 8 ± 1 ng g^{-1} ww (smoked salmon, F2) and at 4.5 ± 0.9 ng g^{-1} ww (sausage of tuna and salmon, F4), containing the last one 6-B(cd)pyr (0.5 ± 0.1 ng g^{-1} ww) as well. Finally, 5,12-Napht was detected in only one seafood sample (cooked prawns, S2) with the highest concentration (8 ± 1 ng g^{-1} ww). Figures S3 and S4 shows some representative chromatograms.

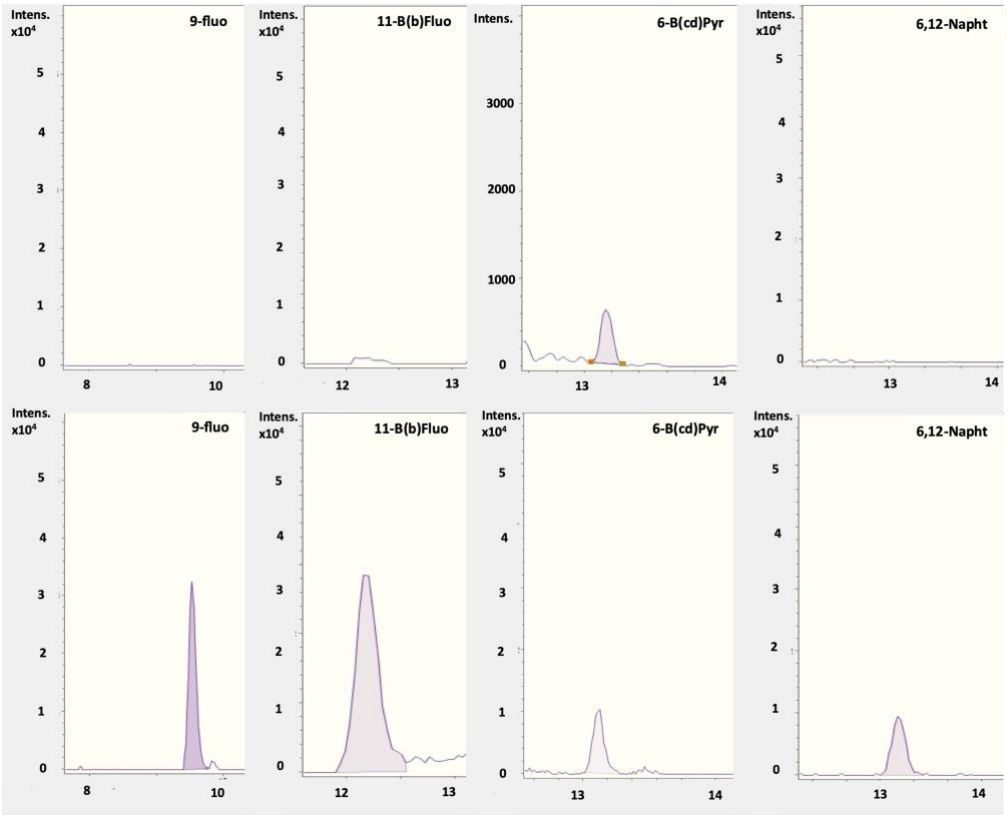


Figure S3. *Extracted ion chromatograms of quantifier ions of target compounds in cooked mussel sample (S7): (up) Unspiked sample in which 6B(cd)pyr was measured at a concentration of 3.5±0.6 ng g^{-1} and (down) spiked sample at 50 ng g^{-1} (all analytes).*

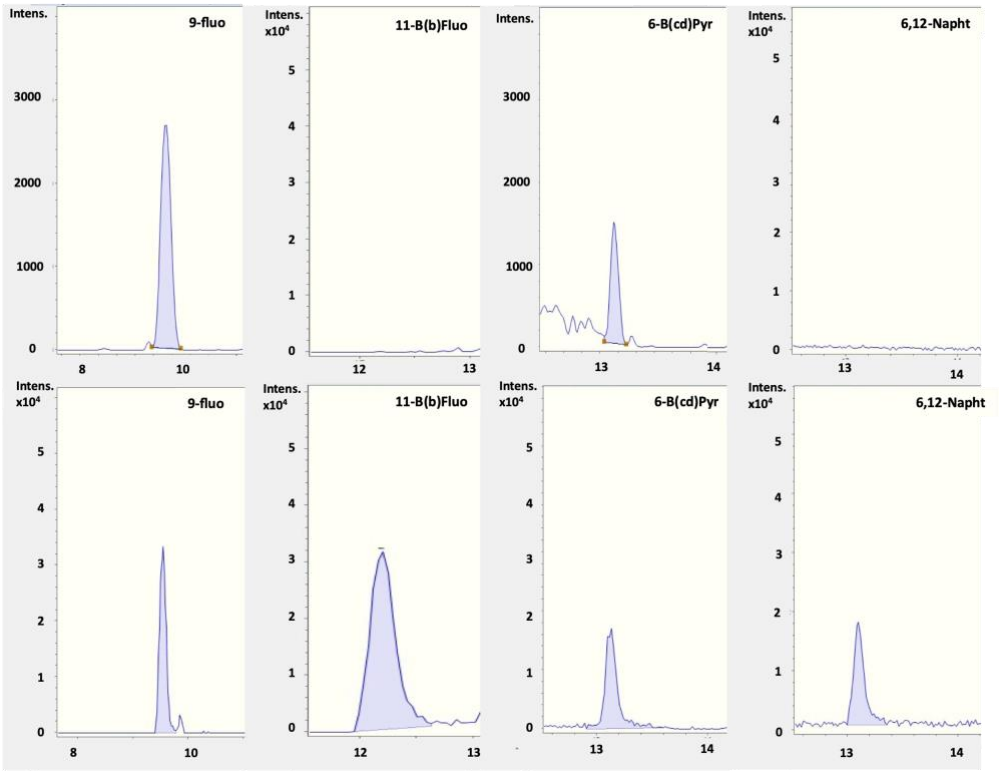


Figure S4. *Extracted ion chromatograms of quantifier ions of target compounds in chicken kebab sample (M7): (up) Unspiked sample in which 7.6±0.1 ng g^{-1} for 9-Fluo and 5±1 for 6-B(cd)pyr were measured and (down) spiked sample at 50 ng g^{-1} (all analytes).*

The Σ oxy-PAHs in fish and seafood samples was in the range 3.5 - 8.6 ng g^{-1} ww. Layshock et al. (2010) found 9-Fluo and 5,12-Napht in a SRM of mussel (22.6 ± 4.9 and 31.9 ± 7.6 ng·g-1 dw, respectively) [Layshock et al., 2010]. These values are comparable to those of our study taking into account that levels were reported in dry weight and that samples contain around 80-90% of water. Higher levels of Σ oxy-PAHs have been reported by Bandowe et al. (2014) (28 to 1,715 ng g^{-1} dw in fish muscle and gut) and by Ranjbar Jafarabadi, A. et al (2019) (40.35-110 ng g^{-1} dw in fish liver and muscle). However, it should be taken into account that these values are in dry weight and that a higher number of oxy-PAHs were monitored, namely 15 and 9, respectively.

Regarding the value of Σ oxy-PAHs in the positive meat sample (M7) (12.6 ng g^{-1} ww, sum of 6-B(cd)pyr and 9-Fluo) this was similar to values reported in other studies, such as 26–62.4 ng g^{-1} ww in beef meat (sum of 9-Fluo; anthracene-9,10-dione; benzo[a]anthracene-7,12-dione; bezanthrone; 11-B(b)fluo; 5,12-Napht and 6-B(cd)pyr) [Zastrow, Speer, Schwind & Jira, 2021], 8.5 – 80 ng g^{-1} ww in smoked meat (sum of 9-Fluo; anthracene-9,10-dione; benzo[a]anthracene-7,12-dione and benzanthrone) [Chen et al., 2014] or 3.2 ± 0.5 ng g^{-1} ww of anthracene-9,10-dione in sausages [Zastrow, Schwind, Schwagele & Speer, 2019].

4. Conclusions

New green SUPRASs made up of short-medium chain length alcohols (C_6-C_{10}) in mixtures of water and a sustainable solvent (2-MeTHF) were characterized. SUPRASs contained a high amphiphile concentration (63-95%) and a low water percentage (3-10%) allocated in the internal vacuoles of inverse aggregates. These SUPRASs provided a good balance of polar/non-polar interactions for the extraction of medium polar to highly apolar compounds. To prove the suitability of SUPRASs as an alternative to conventional sample preparation methods, SUPRASs treatment was optimized and validated for the determination of oxy-PAHs in processed seafood, fish and meat samples, followed by analysis by liquid chromatography coupled to high resolution mass spectrometry. The method was simple (10 min agitation and 20 min centrifugation), consumed low amounts of reagents (200 µL SUPRAS per sample) and did not required drying the sample or performing repetitive extractions or evaporation/concentration steps. Quantification limits were in the range 0.08 - 4 ng·g^{-1} and total recoveries varied between 70 and 129 (RSD: 0.06-19 %). The method was applied to 19 samples bought in local supermarkets. Oxy-PAHs were found in 7 samples at levels in the range (Σ oxy-PAH: 3.5 - 12.6 ng·g^{-1} ww), mainly in fish and seafood.

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Determination of several PFAS groups in food packaging material from fast-food restaurants in France

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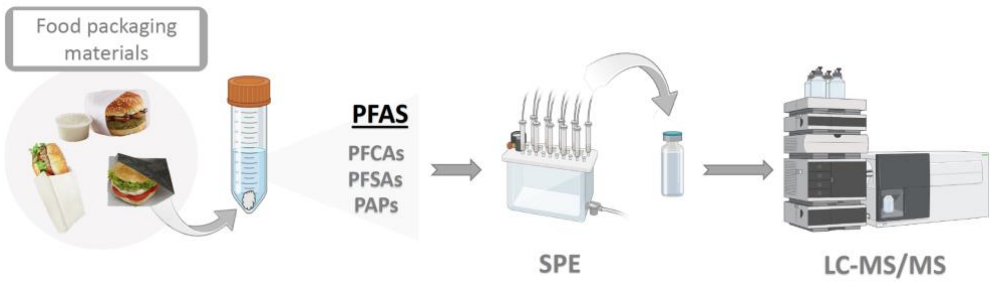

Highlights

- PFAS were quantified in food contact materials from France
- PFHxA, 6:2 FTS and 6:2/6:2 diPAP were found in all samples
- PAPs showed the highest concentrations
- Strong correlations between compounds suggest similar degradation routes or a common origin

Abstract

Per- and polyfluoroalkylated substances (PFAS) are a huge group of toxic compounds which have been widely used in industrial and consumer applications, from where they can migrate into the environment. They can pose a risk to human health because they have been associated with several diseases. To obtain more information on the risk of PFAS in fast food packaging materials, several PFAS (perfluorocarboxylic acids or PFCAs (n=16), perfluorosulfonic acids or PFSAs (n=14), and a miscellaneous group constituted by sulfonamides (n=5) and fluorotelomer phosphate esters or PAPs (n=5)) were quantified in food contact materials (FCMs) from fast-food restaurants. Perfluorohexanoic acid (PFHxA), 6:2 Fluorotelomer sulfonic acid (6:2 FTS) and 6:2/6:2 Fluorotelomer phosphate diester (6:2/6:2 diPAP) were detected in all samples. PFCAs with shorter chain lengths (C4-C6) showed the highest concentrations compared to median (C7-C10) and longer chain length PFCAs (C11-C18). However, they had lower detection frequencies (DFs) (except for PFHxA, DF = 100%) with values of 36 and 34% for C4 and C5 PFCAs, respectively. The DF of longer chain length PFCAs was higher, especially those of the median chain length PFCAs (C8-C10, with DF = 79 – 98%). Analytes from the PFSA group with high DFs (70 – 98%) were perfluorobutane sulfonic acid (PFBS), perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS, linear and branched) and 10:2 Fluorotelomer sulfonic acid (10:2 FTS), with concentrations similar to some analytes from the PFCA group. 4:2 Fluorotelomer phosphate monoester (4:2 mPAP), 8:2 Fluorotelomer phosphate monoester (8:2 mPAP) and 8:2/8:2 Fluorotelomer phosphate diester (8:2/8:2 diPAP) were found with the highest concentrations and DFs ranged 68 – 94%. Some correlations between analytes were found, indicating similar degradation routes or a common origin.

Keywords: *PFAS, PFCAs, PFSAs, PAPs, food contact materials*

1. Introduction.

Per- and polyfluoroalkylated substances (PFAS) are a diverse class of organic compounds with a terminal functional group (e.g., alcohols, carboxylates, sulfonamides, sulfonates) whose hydrogen atoms in the carbon chain have been totally or partially replaced by fluorine atoms, respectively (Buck et al., 2011). Because the carbon-fluorine bond is one of the strongest bonds known in organic chemistry (Banks et al., 2013; Glenn et al., 2021), these chemicals do not degrade even at high temperatures. They are extremely resistant to water and oil simultaneously (Baran, 2001; Glenn et al., 2021; Hepburn et al., 2019). For that reason, they have been widely used in industrial and consumer applications since 1940s, in, among others, hydraulic aviation fluids, paints and inks, fire extinguishing foams, textiles, metals, pesticides, floor polishes, anti-stain coatings, non-stick kitchen utensils or food contact materials (FCMs) (Ateia et al., 2019; Ramírez-Carnero et al., 2021; Trier et al., 2011a). They can migrate from those materials into the environment. This can be a risk for human health, since PFAS have been associated with several types of cancers, immunotoxicity and developmental toxicity (Schaider et al., 2017). Some of them such as the perfluoro alkyl acids (PFAAs) perfluorooctanoic acid (PFOA) or perfluorooctane sulphonic acid (PFOS) have been related to testicular and kidney cancer (Barry et al., 2013) and hypo- and hyperthyroidism (Lopez-Espinosa et al., 2012). Their precursors such as fluorotelomer alcohols (FOTHs) or polyfluoro alkyl phosphate esters (PAPs) have been related with steroidogenesis issues (Rosenmai et al., 2013).

Because of that, the use of PFOA and some related compounds has been regulated by the European chemicals legislation (REACH). They were restricted from 4 July 2020 (European Commission, 2006). Other PFAS, such as PFOS and its salts have been included in the Annex B (persistent organic pollutants, POPs) of the Stockholm Convention (Granby and Tesdal Håland, 2018; Jensen, 2010). Industry reacted by introducing short- (4-7 fully fluorinated carbons) and ultra-short- (2-3 fully

fluorinated carbons) chain PFAS like perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA) and perfluorohexanoic acid (PFHxA) as alternatives (Ramírez-Carnero et al., 2021). These compounds have shorter half-lives in organism (Kjølholt et al., 2015), but they have a higher mobility because they are more water soluble and volatile (Ateia et al., 2019; Glenn et al., 2021; Hernández et al., 2019). They have a similar persistence in the environment. Also, they can migrate more readily from FCMs into the food and are also more easily absorbed upon ingestion (Begley et al. 2005; Schilling Costello and Lee, 2020). In addition, higher quantities of these compounds are needed in comparison to their long-chain homologues to fulfill the same function (Ateia et al., 2019).

Since ingestion, either of contaminated food or drinking water (Glenn et al., 2021), is a very relevant exposure source to toxic contaminants, studies about their presence in FCMs are important. PFAS concentrations in FCMs reported until now and details of the employed analytical methods are shown in Table S1 (supporting information, SI). For example, PFAS (expressed as sum of several perfluorocarboxylic acids, PFCAs, and perfluorosulphonic acids, PFSAs) have been found in popcorn bags beakers [6 – 290 ng·g-1 (Begley et al., 2005), 9.1 ng·g-1 (Dolman and Pelzing, 2011), 159 – 548.7 ng·g-1 (Martínez-Moral and Tena, 2012), 4.3 – 28 ng·g-1 (Moreta and Tena, 2013), 3.5 – 750 ng·g-1 (Moreta and Tena, 2014), 568 ng·g-1 (Zabaleta et al., 2016), 68 – 167 ng·g-1 (Yuan et al., 2016), <LOD – 466 ng·g-1 (Zabaleta et al., 2017), <LOD – 1.3 ng·g-1 (Granby and Tesdal Håland, 2018), <LOD – 28.6 ng·g-1 (Monge Brenes et al., 2019) and 2.1 – 115.7 ng·g-1 (Zabaleta et al., 2020)]. Popcorn bags and beakers are the most studied FCMs with the highest PFAS concentrations. PAPs (as sum of several monoPAPs and diPAPs) were also found in these FCMs in the same order of magnitude or lower [0.5 - 4.2 ng·g-1 (Gebbink et al., 2013), 12.1 – 15.4 ng·g-1 (Zabaleta et al., 2016) and <LOD – 112 ng·g-1 (Zabaleta et al., 2017)]. Other FCMs in which PFAS and PAPs have been found are paper and cardboard boxes, [<LOQ – 5.1 ng·g-1 (Yuan et al., 2016) and 0.03 ng·g-1 (Granby and Tesdal Håland, 2018) for PFAS and 0.6 – 1 ng·g-1 (Gebbink et al., 2013), and 7.3 ng·g-1 (Zabaleta et al., 2016)

for PAPs] or wrapping packages [84.7 ng·g-1 (Zafeiraki et al., 2014) for PFAS, and 0.3 – 1.2 ng·g-1 (Gebbink et al., 2013) and 11 ng·g-1 (Zabaleta et al., 2020) for PAPs]. In other FCMs, such as beakers of paper and cardboard, only PAPs were found [0.2 – 9 ng·g-1 (Gebbink et al., 2013) and 2.1 ng·g-1 (Zabaleta et al., 2020)].

The presence of PFAS in FCMs can be explained in different ways. These products may come from other countries outside the U.S. or Europe, such as Asia, where long-chain PFAS (>C8) are still used in FCMs (Zabaleta et al., 2017). Also, some of these studies are older and were carried out before regulations came in place or were done during the phase out of some PFAS. Since 1967, the U.S. Food and Drugs Administration (FDA) has listed 90 different PFAS permitted for use in FCMs. That list was reduced over the years to less than one third (Glenn et al., 2021). Finally, some studies have demonstrated that some PFAS such as PAPs degrade to PFCAs (Butt et al., 2014; Chen et al., 2019), in that way adding to the PFCA concentration in FCMs. D'eon and Mabury (2007) demonstrated biotransformation of 8:2 Fluorotelomer phosphate monoester (8:2 mPAP) and 8:2/8:2 Fluorotelomer phosphate diester (8:2/8:2 diPAP) into PFOA and possibly also into perfluoroheptanoic acid (PFHpA). However, sometimes PFCAs are found in trace levels because they can come from recycle processes or are residual impurities of technical blends of polymers, so they are considered as non-intentionally added substances (NIAS) (Trier et al., 2018). For example, PFOS is found as an impurity in some grease-proof paper coatings and PFOA is sometimes found because it was added as processing aid in the PTFE manufacture (Begley et al., 2005).

The objective of this work was to obtain a better impression of a large range of PFAS in fast food contact materials. Therefore, several groups of PFAS [sixteen PFCAs (C4 – C18), fourteen PFSA (C4 – C10, five sulfonamides (C8) and five PAPs (C4 – C20)] were quantified in FCMs that were collected in French fast-food restaurants. In addition to PAPs, that were expected to be frequently used in FCMs (Posner et al., 2013; Trier et

al., 2011a, 2011b), we included a range of short-chain PFAS (<C6), which are of high concern based on their large mobility in the environment (Pike et al., 2021) but for which concentrations in FCMs were only scarce.

Table S1. Reported presence of PFAS in food pacaking material: target compounds, concentration range (ng g^{-1}), detection (LOD) and quantification (LOQ) limits (ng g^{-1}), packaging material and contained food, with sample preparation method.

[a]Analytes	PFAS concentration (Σ, ng g^{-1})	PAP concentration (Σ, ng g^{-1})	[b]Contained food (type of material)	LOD (ng g^{-1})	LOQ (ng g^{-1})	Sample preparation	Ref.
PFBA, PFPeA, **PFHxA, PFHpA,** PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeA, PFHxDA, PFODA, PFBS, PFPeS, PFHxS, PFHpS, PFOS, PFNS, PFDS, PFOSA, N-MeFOSA, N-EtFOSA, HFPO-DAM 9Cl-PF3ONS, 11Cl-PF3OUDS, **FTS (4:2, 6:2,** 8:2, **10:2),** mPAP (6:2, 8:2), **diPAP (6:2/6:2, 8:2/8:2)**	< LOQ – 14 < LOD < LOD	< LOQ – 290 < LOD < LOD	13 Oil-beading compostable 15 Oil-beading takeaway paper 14 Oil-spreading or oil-soaking paper/board	-	1700 (PFAS) 26.000-260.000 (PAPs)	LLE **Solvent:** MeOH: Ethyl acetate **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Straková et al., 2021)
PFBS, **PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA,** PFHxS, PFOS, PFOSA, mPAP (6:2, 8:2), **diPAP (6:2/6:2, 8:2/8:2)**	<LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD 2.1 115.7 3282	<LOD 2.1 7 < LOD 2.2 11 < LOD < LOD < LOD < LOD < LOD < LOD < LOD	2 cardboards 1 baking paper 1 muffin cup 1 plate (cardboard) 1 cup (cardboard) 1 burger wrapper 2 boxes 2 French fries wrappes 2 Burger clam bags 1 bag 2 pizza boxes 2 Spanish popcorn bags 1 Chinese popcorn bag 1 pet food bag (paper)	1.3 – 3.5 (PFAS) 0.8 - 2.8 (PAPs)	-	FUSLE **Solvent:** ACN: water (9:1) **extraction time:** 5 min **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Zabaleta et al., 2020)

PFOA PFOS	< LOD – 28.6 < LOD	-	7 popcorn bags (paper) 3 lunch snacks (paper)	0.63 - 1.53 (PFAS)	2.11 – 5.11 (PFAS)	FUSLE **Solvent:** ethanol **extraction time:** 30s **clean-up:** filtration **evaporation/reconstitution steps:** yes	(Monge Brenes et al., 2019)
PFBA, **PFPeA**, **PFHxA**, **PFHpA**, **PFOA**, **PFNA**, **PFDA**, **PFUnDA**, **PFDoDA**, **PFTrDA**, **PFTeA**, PFBS, PFHxS, **PFOS**, PFDS, PFOSA, mPAP (6:2, 8:2), diPAP (6:2/6:2, 8:2/8:2)	< LOD – 10.3 < LOD – 0.746 < LOD – 0.8 < LOD – 0.021 < LOD - 1.3 < LOD < LOD < LOD 0.025 < LOD < LOD	< LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD < LOD	11 plates (different materials) 5 cupcake cups 5 food bags (paper) 3 hot drink cups 3 popcorn beakers 2 candy bags (paper) 2 baking paper 1 coffee filter 1 pizza tray 1 French fries tray 1 snack beaker (cardboard)	0.006 – 0.06 (PFAS) 0.006 (PAPs)	-	PLE **Solvent:** ethanol and ethanol:water **extraction time:** 1 h **clean-up:** filtration **evaporation/reconstitution steps:** no	(Granby and Tesdal Haland, 2018)
PFBA, **PFPeA**, **PFHxA**, **PFHpA**, **PFOA**, **PFNA**, **PFDA**, PFUnDA, PFDoDA, PFTrDA, PFTeDA, PFBS, PFHxS, PFOS, PFOSA, PFHxPA, **mPAP (6:2, 8:2), diPAP (6:2/6:2, 8:2/8:2,** 10:2/10:2), triPAP (6:2/6:2/6:2)	< LOD – 466	< LOD - 112	33 popcorn bags (cardboard)	1.3 – 3.5 (PFAS) 0.8 – 2.8 (PAPs)	-	FUSLE **Solvent:** methanol **extraction time:** 2.5 min **clean-up:** filtration and SPE **evaporation/reconstitution steps:** yes	(Zabaleta et al., 2017)
PFBS, **PFHxS**, **PFOS**, PFDS, PFBA, **PFPeA**, **PFHxA**, **PFHpA**, **PFOA**, **PFNA**, **PFDA**, **PFUnDA**, **PFDoDA**, PFOSA, **N- EtFOSA**, **N-MeFOSA**, **mPAP (6:2, 8:2),** diPAP (6:2/6:2, 8:2/8:2)	< LOD – 306.44	< LOD - 478	Burger wrapper (paper) French fries box (paper) pizza box (paper) sandwich box (paper) non-stick baking cup popcorn bag soup cup	0.004 - 0.03 (PFAS) 4.5 - 119 (PAPs)	-	PLE **Solvent:** diluted acetic acid and methanolic ammonium hydroxide **extraction time:** 90 min **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Shoeib et al., 2016)

PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, **PFDA**, PFBS, PFHxS, PFOS, PFOSA, PFHxPA, mPAP (6:2, 8:2), **diPAP (6:2/6:2, 8:2/8:2)**	568 < LOD < LOD < LOD	12.1 7.3 < LOD 15.4	Popcorn bag (cardboard) Pizza box (cardboard) French fries wrapper (cardboard) Popcorn box (cardboard)	0.002 – 0.05 (PFAS) 0.0005 – 0.35 (PAPs)	0.005 – 0.25 (PFAS) 0.0025 – 1.15 (PAPs)	PLE **Solvent:** methanol (1% acetic acid) **extraction time:** 2.5 min **clean-up:** filtration **evaporation/reconstitution steps:** yes	(Zabaleta et al., 2016)
PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoA, PFTrDA, PFTeDA, PFHxDA, FODA	< LOQ – 186 68 – 167 < LOQ – 5.59 < LOQ – 17.2 < LOQ – 5.1 < LOQ – 4.88 < LOQ - 33	-	16 tableware (paper) 6 popcorn bags 9 cupcake cups 6 cups (paper) 12 boxes (paper) 11 bags (paper) 9 others (paper)	-	0.08 – 0.43 (PFAS)	PLE **Solvent:** methanol **extraction time:** 3 h **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Yuan et al., 2016)
PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoA, PFOS	3.5 – 750	-	6 Popcorn bags (paper)	0.2 – 0.4 (PFAS)	0.4 – 1.6 (PFAS)	FUSLE **Solvent:** ethanol **extraction time:** 10s **clean-up:** filtration **evaporation/reconstitution steps:** yes	(Moreta and Tena, 2014)
PFBA, PFPeA, **PFHxA** **PFHpA**, PFOA, **PFNA**, **PFDA**, PFUnDA, **PFDoDA**, **PFTrDA**, **PFTeDA**, PFHxDA, FODA, PFBS, PFHxS, PFOS, PFDS	< LOD < LOD < LOD 84.72 < LOD 622.24	-	8 beverage cups 1 ice cream cup 8 fast food boxes (paper) 8 fast food wrappers 2 materials for baking (paper) 3 microwave bags (paper)	0.2 – 2.65 (PFAS)	0.54 – 2.83 (PFAS)	PLE **Solvent:** methanol **extraction time:** 21 min **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Zafeiraki et al., 2014)
PFHpA, PFOA, PFNA, **PFDA**, PFUnDA, **PFDoDA, PFOS**	4.3 – 28 15.5 6.1	-	6 popcorn bags (paper) 1 cup (cardboard) 1 Ice cream tub	0.5 – 2.2 (PFAS)	1.4 – 7 (PFAS)	FUSLE **Solvent:** ethanol **extraction time:** 10 s **clean-up:** filtration **evaporation/reconstitution steps:** yes	(Moreta and Tena, 2013)

mPAP (6:2, 8:2, 10:2), **diPAP (6:2/6:2, 8:2/8:2, 10:2/10:2)** triPAP (6:2/6:2/6:2),	-	0.53 – 4.19 0.56 0.11 0.33 - 0.81 1.2 < LOD 9.02 0.17 0.6 0.99 0.23	3 popcorn bags (paper) 1 Thai food box (cardboard) 1 Gorbys pirogue (paper) 2 pizza wrapping (paper) 1 apple pie wrapping (paper) 1 cup (cardboard) 1 French fries (paper) 1 muffing baker (paper) 1 burger box (cardboard) 1 burger box (paper) 1 French fries (cardobard)	-	-	PLE **Solvent:** methanol **extraction time:** 8 h **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Gebbink et al., 2013)
PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFOS	159 – 548.7	-	3 popcorn bags (paper)	0.7 – 18 (PFAS)	2 – 53 (PFAS)	PLE **Solvent:** methanol **extraction time:** 6 min **clean-up:** no **evaporation/reconstitution steps:** no	(Martínez-Moral and Tena, 2012)
PFHxA, PFHpA, **PFOA,** PFNA, PFDA, PFUnDA, PFOS	< LOD 9.1 < LOD < LOD	-	2 non-stick baker (paper) 2 popcorn bags 1 French fries box 1 sandwich wrapper	0.5 (PFAS)	1 (PFAS)	PLE **Solvent:** water **extraction time:** 1 h **clean-up:** SPE **evaporation/reconstitution steps:** yes	(Dolman and Pelzing, 2011)
mPAP (4:2, 6:2, 8:2, 10:2), **diPAP (4:2/4:2, 6:2/6:2, 8:2/8:2, 10:2/10:2)**, triPAP (x:2/y:2/z:2), **PFOS**, **PFOA**, PFSA, PFOSA, N-EtFOSA	< LOQ	< LOQ < LOQ < LOD < LOD < LOD < LOD < LOD < LOD < LOD	6 Popcorn bags (paper) 1 burguer box (cardboard) 1 chocolate cake bag (paper) 1 bread bag (paper) 1 panang curry chicken (cardobard) 1 lasagne Bolognese (cardboard) 1 fast noodles (cardboard)	0.008-0.2 mg/L (PFAS) 0.2 – 1.81 mg/L (PAPs)	-	PLE **Solvent:** ethanol 95% **extraction time:** 2h **clean-up:** centrifugation and filtration **evaporation/reconstitution steps:** no	(Trier et al., 2011)
PFOA	6 – 290 < LOD < LOD < LOD < LOD	-	1 Popcorn bag (paper) 1 burger wrapper 1 sandwich wrapper 1 French fries box 1 plate (paper)	-	-	PLE **Solvent:** ethanol:water **extraction time:** 60 min **clean-up:** filtration **evaporation/reconstitution steps:** no	(Begley et al., 2005)

[a]Analytes detected in samples are shown in bold. [b]Type of material is described in brackets. No information means that type of material is not specified in the article. Analysis technique was LC-MS for all of them. FUSLE: focused ultrasound solid-liquid extraction; PLE: pressurized liquid extraction; SPE: solid phase extraction. References:

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2. Materials and methods.

2.1. Chemicals and reagents.

Solvents were methanol (MeOH), acetonitrile (ACN), tetrahydrofuran (THF), obtained from Bisolve Chimie SARL (Dieuze,

France). Acetic acid was also obtained from Bisolve Chimie SARL, while ammonia solution (NH4OH) was purchased from Supelco, Merck (Darmstadt, Germany). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain). Target compounds are shown in Table S2 (SI). They have been classified in groups: PFCAs (16), PFSAs (14) and a miscellaneous group constituted by sulfonamides (5) and PAPs (5). A spike solution (100 ng·mL-1 for PAPs and 10 ng·mL-1 for the other analytes) was prepared in MeOH and stored at -20 ºC. The employed deuterated and ^{13}C labeled internal standards (ISs) are shown in Table S3 (SI). The solution of ISs (concentration of individual compounds were in the range 6.5 - 10.9 ng·mL-1) was also prepared in MeOH and stored at -20 ºC.

Table S2. Target compounds in this study

Analyte	Acronym	CAS
Perfluorobutanoic acid	**PFBA**	375-22-4
Perfluoropentanoic acid	**PFPeA**	2706-90-3
Perfluorohexanoic acid	**PFHxA**	307-24-4
Perfluoroheptanoic acid	**PFHpA**	375-85-9
Perfluorooctanoic acid (linear)	**PFOA**	335-67-1
Perfluorooctanoic acid (branched)	**PFOA Br**	335-67-1
Perfluorononanoic acid	**PFNA**	375-95-1
Perfluorodecanoic acid	**PFDA**	335-76-2
Perfluoroundecanoic acid	**PFUnDA**	2058-94-8
Perfluorododecanoic acid	**PFDoDA**	307-55-1
Perfluorotridecanoic acid	**PFTrDA**	72629-94-8
Perfluorotetradecanoic acid	**PFTeDA**	376-06-7
Perfluorohexadecanoic acid	**PFHxDA**	67905-19-5

Perfluorooctadecanoic acid	**PFODA**	16517-11-6
Hexafluoropropylene oxide dimer acid	**HFPO-DA**	13252-13-6
Dodecafluoro-3H-4,8-dioxanonanoate	**DONA**	958445-44-8
Perfluorobutane sulfonic acid	**PFBS**	375-73-5
Perfluoropentane sulfonic acid	**PFPeS**	2706-91-4
Perfluorohexane sulfonic acid	**PFHxS**	355-46-4
Perfluoroheptane sulfonic acid	**PFHpS**	375-92-8
Perfluorooctane sulfonic acid (linear)	**PFOS**	1763-23-1
Perfluorooctane sulfonic acid (branched)	**PFOS Br**	1763-23-1
Perfluorononane sulfonic acid	**PFNS**	68259-12-1
Perfluorodecane sulfonic acid	**PFDS**	335-77-3
9-chlorohexadecafluoro-3-oxanonane-1-sulfonate	**9ClPF3OUdS**	756426-58-1
11-chloroeicosafluoro-3-oxaundecane-1sulfonate	**11ClPF30UdS**	763051-92-9
4:2 Fluorotelomer sulfonic acid	**4:2 FTS**	757124-72-4
6:2 Fluorotelomer sulfonic acid	**6:2 FTS**	27619-97-2
8:2 Fluorotelomer sulfonic acid	**8:2 FTS**	39108-34-4
10:2 Fluorotelomer sulfonic acid	**10:2 FTS**	120226-60-0
Perfluorooctane sulfonamide	**PFOSA**	754-91-6
N-Methylperfluorooctane sulfonamide	**N-MeFOSA**	31506-32-8
N-Methylperfluorooctanesulfonamidoacetic acid	**N-MeFOSAA**	2355-31-9
N-ethylperfluorooctane sulfonamide	**N-EtFOSA**	4151-50-2
N-Ethylperfluorooctanesulfonamidoacetic acid	**N-EtFOSAA**	2991-50-6
4:2 Fluorotelomer phosphate monoester	**4:2 mPAP**	150065-76-2
6:2 Fluorotelomer phosphate monoester	**6:2 mPAP**	57678-01-0
8:2 Fluorotelomer phosphate monoester	**8:2 mPAP**	57678-03-2
6:2/6:2 Fluorotelomer phosphate diester	**6:2/6:2 diPAP**	57677-95-9
8:2/8:2 Fluorotelomer phosphate diester	**8:2/8:2 diPAP**	678-41-1

Table S3. MRM transitions, declustering potential and collision energy. Quantifiers for PFAS are indicated in bold.

	Precursor	Product ion	Declustering potential (V)	Collision energy (V)
PFBA	212.8	169	-10	-12
PFBA ^{13}C4	216.8	172	-10	-12
PFPeA	262.8	218.7	-10	-14
PFPeA	262.8	69.2	-10	-52
PFPeA ^{13}C5	267.8	223	-10	-14
PFHxA	312.8	268.9	-10	-14
PFHxA	312.8	119	-10	-28
PFHxA ^{13}C5	317.8	272.9	-10	-14
PFHpA	362.8	319.1	-10	-14
PFHpA	362.8	169.1	-10	-24
PFHpA ^{13}C4	366.8	322.1	-10	-14
PFOA	412.8	368.9	-10	-16
PFOA	412.8	169	-10	-26
PFOA ^{13}C8	420.8	375.9	-10	-16
PFOA Br[a]	412.8	368.9	-10	-16
PFNA	462.9	419.1	-10	-16
PFNA	462.9	219.1	-10	-26
PFNA ^{13}C9	471.9	427.1	-10	-16
PFDA	512.8	468.9	-10	-18
PFDA	512.8	218.9	-10	-26
PFDA ^{13}C6	518.8	473.9	-10	-18
PFUnDA	562.8	519.1	-45	-18
PFUnDA	562.8	268.7	-45	-26
PFUnDA ^{13}C7	569.8	525.1	-45	-18
PFDoDA	612.8	568.8	-15	-20
PFDoDA	612.8	318.9	-15	-28
PFDoDA ^{13}C2	614.8	569.8	-15	-20
PFTrDA	662.8	618.8	-35	-18
PFTrDA[a]	662.8	169	-35	-36
PFTeDA	712.8	668.8	-35	-22
PFTeDA	712.8	368.9	-35	-34
PFTeDA ^{13}C2	714.8	669.8	-35	-22

Table S3 (continuation).

	Precursor	Product ion	Declustering potential (V)	Collision energy (V)
PFHxDA	812.7	768.8	-35	-34
PFHxDA	812.7	218.9	-35	-14
PFHxDA ^{13}C2	814.7	769.8	-35	-34
PFODA[a]	912.7	868.8	-65	-26
PFODA	912.7	168.9	-65	-40
HFPO-DA	284.8	168.9	-10	-12
HFPO-DA	284.8	184.9	-10	-24
HFPO-DA ^{13}C3	286.8	168.9	-10	-12
DONA[a]	376.9	250.9	-10	-16
DONA	376.9	85	-10	-36
PFBS	298.8	79.9	-10	-64
PFBS	298.8	98.9	-10	-36
PFBS ^{13}C3	301.8	79.9	-10	-64
PFPeS[a]	348.8	80	-10	-72
PFPeS	348.8	98.9	-10	-40
PFHxS	398.9	80	-10	-88
PFHxS	398.9	99.1	-10	-64
PFHxS ^{13}C3	401.9	80	-10	-88
PFHpS[a]	448.8	79.9	-10	-100
PFHpS	448.8	98.9	-10	-78
PFOS	498.8	79.8	-10	-92
PFOS	498.8	98.9	-10	-92
PFOS ^{13}C8	506.8	79.8	-10	-92
PFOS Br[a]	498.8	79.8	-10	-92
PFOS Br	498.8	98.9	-10	-92
PFNS[a]	548.8	79.8	-155	-114
PFNS	548.8	98.9	-155	-116
PFDS[a]	598.8	80.1	-65	-116
PFDS	598.8	98.9	-65	-116
9ClPF3OUdS[a]	530.8	350.8	-35	-38
11ClPF30UdS[a]	630.8	450.9	-80	-40
4:2 FTS	326.8	80.9	-10	-54
4:2 FTS	326.8	306.8	-10	-34
4:2 FTS ^{13}C2	328.8	80.9	-10	-54

Table S3 (continuation).

	Precursor	Product ion	Declustering potential (V)	Collision energy (V)
6:2 FTS	426.9	407	-10	-34
6:2 FTS	426.9	81	-10	-62
6:2 FTS ^{13}C2	428.9	81	-10	-62
8:2 FTS	526.8	81	-10	-34
8:2 FTS	526.8	506.7	-10	-34
8:2 FTS ^{13}C2	528.8	80.9	-10	-94
10:2 FTS	626.9	606.7	-5	-44
10:2 FTS	626.9	81	-5	-140
10:2 FTS ^{13}C2	632.9	611.8	-5	-44
PFOSA	497.8	77.9	-10	-88
PFOSA ^{13}C8	505.8	77.9	-10	-88
N-MeFOSA	511.8	218.9	-10	-34
N-MeFOSA	511.8	169.1	-10	-36
N-MeFOSA d3	514.8	218.9	-10	-34
N-MeFOSAA	569.8	418.9	-10	-28
N-MeFOSAA	569.8	511.8	-10	-30
N-MeFOSAA d3	572.8	418.9	-10	-34
N-EtFOSA	525.9	218.9	-55	-36
N-EtFOSA	525.9	168.9	-55	-38
N-EtFOSA d5	530.9	218.9	-55	-36
N-EtFOSAA	583.9	418.9	-10	-30
N-EtFOSAA	583.9	525.8	-10	-30
N-EtFOSAA d5	588.9	418.9	-10	-30
4:2 mPAP[a]	342.8	79	-55	-80
4:2 mPAP	342.8	97.1	-55	-18
6:2 mPAP[a]	442.8	78.9	-65	-110
6:2 mPAP	442.8	97	-65	-18
8:2 mPAP[a]	542.8	78.9	-85	-104
8:2 mPAP	542.8	97	-85	-50
6:2/6:2 diPAP	788.8	78.8	-190	-142
6:2/6:2 diPAP	788.8	443	-190	-30
6:2/6:2 diPAP ^{13}C4	792.8	79	-135	-180

Table S3 (continuation).

	Precursor	Product ion	Declustering potential (V)	Collision energy (V)
8:2/8:2 diPAP	988.8	79.1	-155	-178
8:2/8:2 diPAP	988.8	543.1	-155	-36
8:2/8:2 diPAP $^{13}C4$	992.7	79	-155	-178

2.2. Instrumentation.

The separation of the target compounds was carried out using an Exion LC from Sciex (Framingham, Massachusetts, USA) with a XBridge BEH C18 XP Column (2.1 mm x 150 mm, 2.5 µm particle size) from Waters (Mildred, Massachusetts USA), which was specifically designed for high pH, preceded by a delay Isolator column (2.1 mm x 100 mm) also from Waters. The LC system was coupled to a Sciex 6500+ Triple Quadrupole mass spectrometer equipped with an ESI source operating in negative mode.

Other instruments used for sample treatment were a manifold from Waters, a vacuum pump from ABM (Germany) and ENVICarb cartridges (500mg, 6mL, pk of 30) from Supelco Sigma-Aldrich (St. Louis, USA) used for the SPE process, an ultrasonic bath from Branson (Carouge, Switzerland) which was used for extraction, and a heating plate from IKA RCT basic (Staufen, Germany) that was used for evaporation.

2.3. Analysis of PFAS in food packaging material

2.3.1. Sample collection and treatment

FCMs (n= 47) were collected from several fast-food restaurants from different locations in France, between September and November of

2021. Detailed sampling information is given in Table 1. Leftovers were thoroughly removed from the FCMs in order to avoid rot on the paper and to avoid cross-contamination of PFAS that might have already been absorbed in the FCM from the food. However, the contact times between the food and the FCM was kept to less than 1-2 min, so we assume that neither major losses of the FCM to the food have taken place nor transfer from the food to the FCM. The samples were stored individually in a plastic sleeve and sent to Amsterdam for analysis. Once there, they were cut into equal parts of approximately 5 x 5 cm. Only clean parts were taken for analysis.

2.3.2. PFAS extraction and clean-up

The extraction procedure was similar to the method applied by Schaider et al. (2017) with some modifications. Aliquots of approximately 2 g were weighed in 50 mL propylene tubes and 50 □L of the ISs solution (in the range 6.5 – 10.9 ng·mL-1) was added. Samples were extracted twice with 20 mL of MeOH by sonication at room temperature during 30 min each. The two extracts were combined and evaporated to ~0.5 mL under a gentle stream of N2 at 50 °C. The extract was diluted with 1.5 mL MeOH:ACN (1:1, v/v) containing 0.3% of acetic acid and underwent a clean-up step using an ENVI-Carb cartridge (500 mg). Cartridges were previously washed with 5 mL of MeOH and conditioned with 3 mL of MeOH:ACN (1:1, v/v) containing 0.3% of acetic acid. After the sample extract was loaded, the target compounds were eluted with 3 mL of MeOH:ACN (1:1, v/v) containing 0.3% of acetic acid. After that, the extract was evaporated till dryness, reconstituted in 100 µL of MeOH, diluted 1:1 with water and transferred to a chromatographic vial for LC-MS/MS analysis.

Table 1. Sample details: location, type of packaging and contained food.

Fastfood restaurant	Location	Type of packaging (contained food)	Sample ID
1	Bourg Achard (Eure, 27)	Paper bag (Burger)	1
		Wrapping paper (Burger)	2
	Chatelet (Paris, 75)	Wrapping paper (Burger)	3
		Paper bag (French fries)	4
	Cadet (Paris, 75)	Paper bag (Burger)	5
		Wrapping paper (Burger)	6
2	Lescure (Ariege, 09)	Wrapping paper (Burger)	7
		Wrapping paper (Burger)	8
	Eragny (Val-D'oise, 95)	Carrier paper bag	9
		Wrapping paper (Burger)	10
		Wrapping paper (Burger)	11
		Wrapping paper (Burger)	12
	La défense (Hauts-de-Seine, 92)	Wrapping paper (Burger)	13
		Wrapping paper (Burger)	14
		Paper bag (French fries)	15
	13e Arrondissement (Paris, 75)	Wrapping paper (Burger)	16
		Wrapping paper (Burger)	17
		Paper bag (Nuggets)	18
		Wrapping paper (Burger)	19
		Paper bag french fries	20
	Chatelet (Paris, 75)	Paper bag (French fries)	21
		Wrapping paper (Burger)	22
3	Boulogne (Hauts-de-Seine, 92)	Wrapping paper (Burger)	23
		Carrier paper bag	24
		Paper bag (French fries)	25
	Bastille (Paris, 75)	Carrier paper bag	26
		Paper bag (French fries)	27
	Chatelet (Paris, 75)	Paper bag (fried chicken)	28
		Paper bag (French fries)	29
		Paper bag (onion rings)	30
4	Chaussée d'Antin Lafayette (Paris, 75)	Paper bag (pastry)	31
		Paper bag (Burger)	32
		Paper bag (Burger)	33
		Paper bag (pastry)	34
5	Boulogne (Hauts-de-Seine, 92)	Paper bag (pastry)	35
		Paper bag (baguette)	36
	Gare Saint Lazare (Paris, 75)	Paper bag (pastry)	37
		Paper bag (baguette)	38
		Paper bag (pastry)	39
6	Grenelle (Paris, 75)	Wrapping paper (Burger)	40
		Wrapping paper (Burger)	41
		Paper bag (cookie)	42
	Porte d'Orléans (Paris, 75)	Wrapping paper (Burger)	43
		Paper bag (cookie)	44
	Boulevard Voltaire (Paris, 75)	Wrapping paper (Burger)	45
		Wrapping paper (Burger)	46
		Paper bag (cookie)	47

2.3.3. Quantification of PFAS by LC/MS.

The mobile phase used for the PAPs separation was a solution of ammonium acetate 2mM (A) and MeOH 100% (B) at a flow rate of 0.3 mL·min-1. The gradient was as follows: initial 95% of A during 0.5 min, decreasing to 50% A at 2 min, decreasing to 1% A at 10 min, kept constant at 1% A for 8 min and finally, re-conditioning for 5 min. For separation of the other analytes, the mobile phase consisted of a solution of ammonium acetate 2mM (A) and MeOH:ACN (1:1, v/v) (B) at a flow rate of 0.45 mL·min-1. The gradient was initial 90% of A during 0.2 min, decreasing to 40% A at 6 min, decreasing to 5% A at 10 min, kept constant at 1% A for 8 min and finally, re-condition for 5 min.

Optimal source parameters were (for PAPs and the rest of analytes, respectively): gas temperature: 400°C, curtain gas: 30 and 35 psi, nebulizer gas: 55 and 60 psi, heater gas: 65 and 50 psi, capillary voltage: -4500 V and -4000 V. MRM transitions for target compounds and ISs are given in Table S3 (SI). Raw data were controlled and processed using Sciex OS software.

2.4. Method performance evaluation.

The performance of the extraction method was evaluated using a representative sample fortified with the target compounds (2.5 and 0.25 ng·g-1 for PAPs and for the other compounds, respectively) and ISs (0.16 - 0.27 ng·g-1). Solvent procedural blanks neither containing the sample nor the target compounds were also run. Accuracy was expressed as recovery and precision as intra-day relative standard deviation (RSD). Calibration curves (1/x weighed regression, n=7) were prepared in MeOH (see calibration ranges in Table S4, SI) with ISs solution (ranged 0.16 - 0.27 ng·g-1). The limit of detection (LOD) and the limit of quantification (LOQ) were estimated at a signal-to-noise ratio of 3 and 10, respectively (See table S4, SI).

Table S4. Analytical performance

Analytes	Slope ($L \cdot ug^{-1}$) ± Standard error	R^2	LOD ($ng \cdot g^{-1}$)	LOQ ($ng \cdot g^{-1}$)	Calibration range (ppb)
PFBA	0.382 ± 0.004	0.9977	0.005	0.020	0.04 – 29.19
PFPeA	0.2756 ± 0.0004	0.9999	0.005	0.020	0.04 – 29.19
PFHxA	0.3886 ± 0.0006	0.9998	0.0025	0.008	0.04 – 29.19
PFHpA	0.402 ± 0.004	0.9978	0.0025	0.008	0.04 – 29.19
PFOA	0.3828 ± 0.0018	0.9993	0.0025	0.008	0.04 – 29.19
PFOA br	0.34 ± 0.004	0.9961	0.0025	0.008	0.04 – 29.19
PFNA	0.4082 ± 0.0014	0.9998	0.0025	0.008	0.04 – 29.19
PFDA	0.4318 ± 0.0016	0.9999	0.0025	0.008	0.04 – 29.19
PFunDA	0.434 ± 0.004	0.9996	0.0025	0.008	0.04 – 29.19
PFDoDA	0.336 ± 0.008	0.9934	0.0025	0.008	0.04 – 29.19
PFTrDA	0.238 ± 0.01	0.9898	0.0025	0.008	0.04 – 29.19
PFTeDA	0.394 ± 0.008	0.9942	0.0025	0.008	0.04 – 29.19
PFHxDA	0.338 ± 0.002	0.9983	0.0025	0.008	0.04 – 29.19
PFODA	0.204 ± 0.0002	0.9893	0.005	0.020	0.04 – 29.19
HFPO-DA	0.367 ± 0.0002	0.9999	0.0005	0.002	0.03 – 26.84
DONA	1.608 ± 0.004	0.9998	0.0005	0.002	0.016 – 12.08
PFBS	0.494 ± 0.002	0.9999	0.0025	0.008	0.03 – 25.84
PFPeS	0.4318 ± 0.0018	0.9991	0.0025	0.008	0.04 – 27.44
PFHxS	0.442 ± 0.002	0.9995	0.0025	0.008	0.04 – 27.59
PFHpS	0.486 ± 0.0014	0.9998	0.0025	0.008	0.04 – 27.73
PFOS	0.4732 ± 0.0016	0.9997	0.0025	0.008	0.04 – 27.88
PFOS br	0.464 ± 0.004	0.9993	0.0025	0.008	0.04 – 27.88
PFNS	0.478 ± 0.006	0.9966	0.0025	0.008	0.04 – 28.03
PFDS	0.258 ± 0.01	0.9761	0.0025	0.008	0.04 – 28.17
9Cl-PF3ONS	3.66 ± 0.12	0.9949	0.005	0.020	0.03 – 26.20
11Cl-PF3OUdS	1.306 ± 0.012	0.9977	0.005	0.020	0.04 – 29.52
4:2 FTS	0.544 ± 0.004	0.9988	0.005	0.020	0.02 – 18.56
6:2 FTS	0.986 ± 0.01	0.9981	0.0025	0.008	0.02 – 17.98
8:2 FTS	0.452 ± 0.006	0.9992	0.005	0.020	0.03 – 27.09
10:2 FTS	0.332 ± 0.0018	0.9996	0.0025	0.008	0.04 – 27.92
PFOSA	0.434 ± 0.016	0.9768	0.005	0.020	0.04 – 29.09
N-MeFOSA	0.382 ± 0.01	0.9999	0.005	0.020	0.03 – 26.09
N-MeFOSAA	0.436 ± 0.012	0.9906	0.0025	0.008	0.02 – 17.53
N-EtFOSA	0.478 ± 0.004	0.9988	0.005	0.020	0.03 – 26.92
N-EtFOSAA	0.4 ± 0.004	0.9987	0.0025	0.008	0.03 – 26.92
4:2 mPAP	0.014 ± 0.0004	0.9978	0.0084	0.0281	0.03 – 63.41
6:2 mPAP	0.02 ± 0.0004	0.9952	0.0027	0.0091	0.03 – 62.11
8:2 mPAP	0.08 ± 0.0016	0.9913	0.0017	0.0057	0.06 – 128.66
6:2/6:2 diPAP	0.06 ± 0.00006	0.9999	0.0001	0.0004	0.02 – 56.49
8:2/8:2 diPAP	0.0018 ± 0.0014	0.9985	0.0009	0.0029	0.03 – 65.64

2.5. Statistical analysis.

Spearman correlation was used to investigate correlations between analytes due to data was not normally distributed after logarithm transformation (Shapiro-Wilks tests were used to investigate the normal distribution of data). Results with $p<0.05$ were considered statistically significant. For statistical purposes, levels below LOQ were replaced with their semi-quantitative value and levels below LOD were replaced by the formula $\sqrt{2}/(2*LOD)$ (Antweiler, 2015).

3. Results and discussion.

3.1. Analytical performance and validation.

Eight portions of a representative sample were fortified at 2.5 and 0.25 ng·g-1 for PAPs and the rest of analytes, respectively. Accuracy was assessed as relative total recovery. That ranged between 60 - 140% for 93% of the analytes from the PFCAs group, 92.3% from PFSAs group, and 67% from the miscellaneous group. The remaining compounds had a recovery of > 140% (PFBA 165.9%, PFDS 265.2% and 8:2/8:2 diPAP 158.6%) or < 60% (6:2 mPAP 58.2% and 8:2 mPAP 51.6%). Intra-day precision was expressed as RSD and varied in 2.8 – 19.3%, 0.3 – 18.4% and 6 – 17.1% for PFCAs, PFSAs and the miscellaneous group, respectively. Recoveries of individual analytes are shown in the SI (Figure S1, SI).

Calibration curves for each analyte had good linearity in the whole range tested, with R2 between 0.9761 and 0.9999. Method LODs were satisfactory (0.0001 – 0.008 ng·g-1 for PAPs and 0.0005 – 0.005 ng·g-1 for PFAS), and method LOQs (0.0004 – 0.03 ng·g-1 for PAPs and 0.002 – 0.02 ng·g-1 for PFAS) (see Table S4, SI). The LODs were in the same magnitude order than those reported by Granby and Tesdal Håland (2018) [0.006 ng·g-1 for PAPs (6:2 mPAP, 8:2 mPAP, 6:2/6:2 diPAP and 8:2/8:2 diPAP) and 0.006 – 0.06 ng·g-1 for PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA,

PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeA, PFBS, PFHxS, PFOS, PFDS, PFOSA)] and Shoeib et al. (2016) [0.004 – 0.03 ng·g-1 for PFAS (PFBS, PFHxS, PFOS, PFDS, PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFOSA, N- EtFOSA, N-MeFOSA)]. The rest of reported LODs were one or two magnitude orders higher.

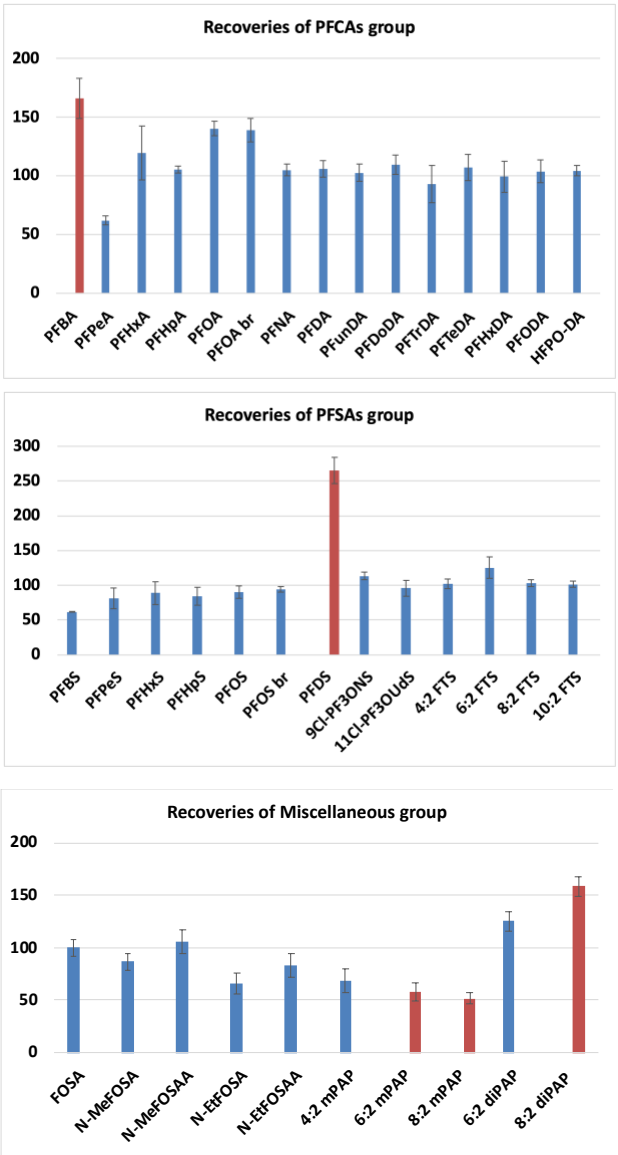

Figure S1. Recoveries in percentage (%) of individual analytes from each group.

To check for background contamination, procedural blanks were added to each sample series. Some analytes were found and the results were corrected for these blank values.

3.2. Analysis of food packaging material.

Table 2 shows the concentration range, mean, median and detection frequency (DF) for each analyte. Concentrations in the individual samples are specified in tables S5-7.

Analytes with a 100% detection frequency (DF) were PFHxA, 6:2 FTS and 6:2/6:2 diPAP, with concentrations ranging from 0.04 to 3.3, 0.01 to 0.1 and 0.01 to 1.9 ng·g-1, respectively.

PFHxA was also detected in samples of microwave popcorn bags by other authors, in concentrations from 174 to 811 ng·g-1 (Zabaleta et al., 2017), 254 ng·g-1 (median concentration) (Zabaleta et al., 2016) and 341 ng·g-1 (median concentration) (Zafeiraki et al., 2014). These concentrations are two orders of magnitude higher than those reported in the present study. In agreement with Lee et al. (2010) these values could be explained by the degradation of other PFAS such as 6:2/6:2 diPAP in PFHxA. This degradation process might cause that PFHxA is frequently present in high concentrations in FCMs. A recent study with microwave popcorn bags reported lower concentrations (2.1 - 12 ng·g-1) (Zabaleta et al., 2020), which are in line with the reported values in the present study and with the Commission Recommendation (EU), which regulates the PFAS presence in food and FCMs (European Commission, 2022). PFHxA has also been found in other types of materials, such as wrapping paper [<LOD – 19.2 ng·g-1 (Zafeiraki et al., 2014) and <LOD – 27 ng·g-1 (Shoeib et al., 2016)] or ice cream cups [25 ng·g-1 (Zafeiraki et al., 2014)], being one order of magnitude higher than our results.

Table 2. Concentration range, mean and median (ng·g^{-1}) and detection frequency (%) of PFAS in food packaging material.

	Concentration range (ng·g^{-1})	Mean (ng·g^{-1})	Median (ng·g^{-1})	Det. frequency (%)	LOD (ng·g^{-1})	LOQ (ng·g^{-1})
PFBA	< 0.004 – 4.1	0.3	< 0.004	36	0.005	0.02
PFPeA	< 0.004 – 1.5	0.09	< 0.004	34	0.005	0.02
PFHxA	0.04 – 3.3	0.3	0.1	100	0.0025	0.008
PFHpA	< 0.002 – 0.5	0.03	< 0.002	28	0.0025	0.008
PFOA	< 0.002 – 0.2	0.05	0.04	87	0.0025	0.008
PFOA br	< 0.002 – 0.2	0.05	0.04	98	0.0025	0.008
PFNA	< 0.002 – 0.09	0.009	0.005*	79	0.0025	0.008
PFDA	< 0.002 – 0.09	0.01	0.007*	91	0.0025	0.008
PFunDA	< 0.002 – 0.07	0.006*	0.003*	55	0.0025	0.008
PFDoDA	< 0.002 – 0.05	0.007*	0.004*	74	0.0025	0.008
PFTrDA	< 0.002 – 0.1	0.02	0.005*	62	0.0025	0.008
PFTeDA	< 0.002 – 0.08	0.02	0.004*	60	0.0025	0.008
PFHxDA	< 0.002 – 0.5	0.03	0.004*	51	0.0025	0.008
PFODA	< 0.004 – 1	0.04	< 0.004	13	0.005	0.02
HFPO-DA	< 0.0004 – 0.02	0.004	0.003	66	0.0005	0.002
DONA	< 0.0004 – 0.002	< 0.0004	< 0.0004	6	0.0005	0.002
PFBS	< 0.002 – 0.2	0.07	0.05	98	0.0025	0.008
PFPeS	< 0.002 – 0.02	0.003*	< 0.002	15	0.0025	0.008
PFHxS	< 0.002 – 1.4	0.2	0.02	91	0.0025	0.008
PFHpS	< 0.002 – 0.03	0.004*	< 0.002	17	0.0025	0.008
PFOS	< 0.002 – 2	0.1	0.03	91	0.0025	0.008
PFOS br	< 0.002 – 2	0.1	0.03	85	0.0025	0.008
PFNS	< 0.002 – 0.04	0.003*	< 0.002	13	0.0025	0.008
PFDS	< 0.002 – 0.007*	0.003*	< 0.002	28	0.0025	0.008
9Cl-PF3ONS	< 0.004	< 0.004	< 0.004	0	0.005	0.02
11Cl-PF3OUdS	< 0.004 – 0.006*	< 0.004	< 0.004	2	0.005	0.02
4:2 FTS	< 0.004 – 0.04	< 0.004	< 0.004	2	0.005	0.02
6:2 FTS	0.01 – 0.1	0.03	0.03	100	0.0025	0.008
8:2 FTS	< 0.004 – 0.1	0.008*	< 0.004	19	0.005	0.02
10:2 FTS	< 0.002 – 0.06	0.006*	0.003*	70	0.0025	0.008
FOSA	< 0.004	< 0.004	< 0.004	0	0.005	0.02
N-MeFOSA	< 0.004 – 0.2	0.008*	< 0.004	2	0.005	0.02
N-MeFOSAA	< 0.002 – 0.01	< 0.002	< 0.002	6	0.0025	0.008
N-EtFOSA	< 0.004 – 0.006*	< 0.004	< 0.004	2	0.005	0.02
N-EtFOSAA	< 0.002 – 0.1	0.008	< 0.004	34	0.0025	0.008
4:2 mPAP	< 0.006 – 42.7	1.6	0.1	94	0.0084	0.028
6:2 mPAP	< 0.002 – 0.7	0.04	< 0.002	34	0.0027	0.009
8:2 mPAP	< 0.001 – 2.7	0.3	0.09	68	0.0017	0.006
6:2/6:2 diPAP	0.01 – 1.9	0.1	0.05	100	0.0001	0.0004
8:2/8:2 diPAP	< 0.001 – 287	19.3	0.2	81	0.0009	0.0029

Mean and median concentrations have been calculated replacing levels below LOQ by their semi-quantitative value and levels below LOD by the formula √2/(2*LOD) (Antweiler, 2015). "<" indicates values under LOD. "*" indicates values under LOQ.

On the other hand, 6:2 FTS was only reported once in a sample of a takeaway paper bag by Schaider et al. (2017), with a concentration of 40 ng·g-1. 6:2 FTS is a ubiquitous compound which has been found in sediments, soil, indoor dust, etc. (Posner et al., 2013). This may be due to other applications of 6:2 FTS than in FCMs. The use of several FTSs is permitted in food packaging materials (Bokkers et al., 2019), so this could explain its presence in all our samples.

Finally, 6:2/6:2 diPAP has been reported in several materials such as microwave popcorn bags (<LOD – 2 ng·g-1) (Zabaleta et al., 2016), muffin cup (7 ng·g-1), cardboard cup (2.2 ng·g-1), baking paper (2.1 ng·g-1) and burger wrapping paper (7 ng·g-1) (Zabaleta et al., 2020), being in the same order of magnitude as our results. Gebbink et al. (2013) reported that 6:2/6:2 diPAP was the most predominant compound in all samples. On the other hand, a recent study reported 6:2/6:2 diPAP as the most prevalent PFAS detected in toilet paper, representing 91% □ 8% on average of the total PFAS concentration (Thompson et al., 2023). In a previous study, high concentrations of 6:2/6:2 diPAP in paper mill wastes streams were reported. Then, it was suggested that diPAP could come from the production process (D'eon et al., 2009). In fact, 6:2/6:2 diPAP it is the main compound of Zonyl®-RP and other Zonyl®-based technical PAP mixtures, usually used in FCM manufacturing (Gebbink et al., 2013).

In terms of ubiquity, the aforementioned compounds were followed by some PFCAs, namely PFOA (linear and branched, br), PFNA, PFDA, PFDoDA, PFTrDA, PFTeDA and HPFO-DA (DF: 60 – 98%) with concentration ranges, means and medians lower than PFHxA and 6:2/6:2 diPAP, but in the same order of magnitude as 6:2 FTS. Shorter chain length PFCAs (C4-C6) showed the highest concentrations (means of 0.3, 0.09, 0.3 ng·g-1, respectively) compared to those of median (C7-C10) and longer chain length PFCAs (C11-C18), which is in agreement with the literature (Ramírez-Carnero et al., 2021; Zabaleta et al., 2017). However, DFs were lower (except for PFHxA, DF= 100%) with values of 36% and 34% for C4 and C5, respectively. The DFs of longer chain length PFCAs

were higher, especially median chain length PFCAs (C7-C10, with DF= 79 - 98%) (See Table 2). PFAS concentrations in microwave popcorn bags were much higher [< LOD – 28.6 ng·g-1 of PFOA (Monge Brenes et al., 2019), 250 – 820 ng·g-1 of PFBA, 15 – 73 ng·g-1 of PFPeA, < LOD – 15 ng·g-1 of PFHpA, 4 – 27 ng·g-1 of PFOA (Zabaleta et al., 2017)], while in other materials such as wrapping papers, concentrations were in the same order of magnitude (< LOD – 3.2 ng·g-1 of PFBA), a bit higher (< LOD - 10 ng·g-1 of PFHpA, < LOD – 5 ng·g-1 of PFNA), or 3 or 4 orders of magnitude higher [< LOD – 28.3 ng·g-1 of PFDA and < LOD – 1,912 ng·g-1 of PFDoDA (Zafeiraki et al., 2014)].

Other analytes with high DFs were from the PFSA group, such as PFBS, PFHxS, PFOS (linear and branched) and 10:2 FTS. PFBS and 10:2 FTS showed DFs ranging from 70 to 98%, and concentration ranges, means and medians in the same order of magnitude as median chain length PFCAs (C8-C10). The other PFSAs had higher concentration ranges, means and medians, similar to PFHxA and 6:2/6:2 diPAP. Monge et al. (2019), Straková et al. (2021), Zabaleta et al. (2016, 2017, 2020) and Zafeiraki et al. (2014) did not detect any PFSA. Granby and Tesdal Håland (2018) quantified PFOS only in a dinner plate (0.01 ng·g-1) and in a pizza tray (0.007 ng·g-1). Shoeib et al. (2016) detected PFOS in 58% of their samples, ranging from < LOD – 5 ng·g-1 in different paper materials and Moreta and Tena (2013) found PFOS in several samples of microwave popcorn bags (< LOD – 5.6 ng·g-1), in a cardboard cup (7.2 ng·g-1) and in an ice cream tub (6.9 ng·g-1). 9Cl-PF3ONS and PFOSA were not found in any sample (DF= 0%), in agreement with other authors such as Granby and Tesdal Håland, (2018), Shoeib et al. (2016), Straková et al. (2021) and Zabaleta et al. (2020).

As expected, PAPs were found in the highest concentrations with DFs ranging from 68 to 94%, except for 6:2 mPAP. This PAP was found in 34% of the samples, with a concentration in the same order of magnitude as median-chain length PFCAs (C7-C10). Concentrations reported in the literature were particularly those of 6:2 mPAP [3 – 27 ng·g-1 in microwave

popcorn bags (Zabaleta et al., 2017) and 196 ng·g-1 in a French fries cardboard box (Shoeib et al., 2016)], 8:2 mPAP [138 - 282 ng·g-1 in two sandwich wrapping papers (Shoeib et al., 2016)] and 8:2/8:2 diPAP [4 ng·g-1 in a burger wrapping paper (Zabaleta et al., 2020)].

Table S5. PFCA concentrations (ng·g^{-1}) in each sample

Sample ID	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFOA br	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA	PFHxDA	PFODA	HFPO-DA	DONA
1	<0	<0	0.04	<0	0.02	<0	*0.004	<0	<0.001	<0.002	*0.003	<0.002	*0.004	*0.02	<0	<0
2	<0	<0	0.2	<0	0.06	<0	*0.008	0.01	*0.004	*0.006	*0.005	*0.004	<0	<0	0.007	*0.002
3	0.3	0.2	0.3	<0	0.05	<0	*0.006	0.02	*0.003	*0.006	*0.004	0.0121	*0.005	<0	0.005	<0
4	0.4	<0	0.1	<0	0.08	0.08	*0.005	0.01	<0.002	*0.004	*0.006	*0.005	<0	<0	0.003	<0
5	<0	<0	0.3	<0	0.04	<0	*0.007	0.01	*0.004	*0.007	*0.005	*0.004	*0.004	<0	0.002	<0
6	0.04	<0	0.06	<0	0.02	0.03	<0.002	<0	<0.0008	<0.001	<0.002	<0.001	<0.002	<0	<0.0004	<0.00006
7	<0	<0	0.06	<0	0.05	0.05	<0	<0	<0	*0.005	<0	<0	<0	<0	<0	<0
8	<0	<0	0.1	<0	0.06	0.06	*0.008	0.0222	*0.003	*0.006	*0.004	*0.003	*0.005	<0	0.007	<0
9	0.1	0.04	0.1	<0	0.06	0.06	0.02	0.03	0.03	0.04	0.07	0.03	0.02	<0	<0	<0.0002
10	<0	<0	0.1	0.02	0.04	0.04	0.01	0.01	0.01	0.02	0.04	0.02	0.02	<0	0.004	<0.0003
11	<0	<0	0.08	<0	0.02	0.02	*0.003	*0.004	*0.003	*0.007	0.02	*0.006	<0	<0	0.003	<0.0002
12	<0	<0	0.3	0.05	0.02	0.03	*0.004	*0.004	<0.002	*0.003	*0.006	<0	<0	<0	0.005	<0
13	<0	<0	0.08	<0	<0	0.07	<0	0.0161	*0.004	*0.004	<0	<0	<0	<0	0.005	<0.0005
14	<0	<0	0.08	<0	0.02	0.02	*0.003	*0.008	*0.003	*0.007	*0.008	*0.004	*0.006	<0	0.002	<0
15	0.5	0.2	0.5	0.08	0.02	0.02	*0.006	*0.003	<0.0006	*0.003	<0	<0	<0	<0	<0	<0
16	<0	<0	0.07	<0	0.02	0.02	*0.004	*0.005	<0.0008	<0.0008	<0	<0	0.01	<0	0.009	<0.0005
17	0.05	<0	0.07	<0	0.02	0.02	*0.005	*0.007	*0.004	0.01	0.05	0.03	0.5	<0	0.005	<0.0003
18	<0	<0	0.6	0.05	0.09	0.1	<0	0.01	<0	<0	<0	<0	<0	<0	0.005	<0
19	<0	*0.01	0.06	*0.007	0.03	0.034	*0.004	0.01	<0.002	0.009	0.06	0.02	0.01	<0	0.002	<0.00009
20	1.2	0.4	2.8	0.3	0.05	0.06	*0.008	0.02	<0	<0	<0	<0	<0	1	<0	<0
21	0.2	0.07	0.6	0.08	0.08	0.09	0.01	0.01	*0.003	<0.002	<0	<0	<0	<0	0.008	<0.0003
22	0.04	<0	0.08	<0	0.1	0.1	*0.007	*0.008	*0.003	*0.005	*0.005	<0.002	0.01	<0	0.01	<0.0003
23	1.4	0.6	3.3	0.5	0.04	0.04	0.009	0.01	<0.002	*0.004	<0	<0	<0	<0	<0	<0.0004
24	0.9	<0	0.2	0.1	0.06	0.07	0.04	0.07	0.03	0.01	<0	<0	<0	<0	<0	<0.0001

25	0.4	<0	0.1	<0	0.2	0.1	0.009	0.01	<0	<0	<0	<0	<0	<0.00002
26	1.4	<0	0.3	<0	0.1	0.1	0.09	0.09	0.07	0.05	0.1	0.05	0.03	<0	<0	<0
27	4.1	<0	0.1	<0	0.2	<0	0.05	<0	<0	<0	<0	<0	<0	<0	<0	
28	0.2	<0	0.6	<0	0.06	<0	*0.007	*0.007	<0	<0	<0	<0	<0	<0	0.01	<0.0002
29	<0	<0	1.1	0.03	0.1	0.2	0.02	0.02	0.01	<0	<0	<0	<0	0.02	*0.001	
30	0.2	<0	0.2	<0	0.1	0.1	0.01	0.009	<0.0001	<0	<0	<0	<0	<0	0.006	<0.0001
31	<0	<0	0.07	<0	0.05	0.05	<0	0.009	*0.003	*0.004	0.008	*0.007	<0	<0	0.005	<0
32	<0	<0	0.1	<0	0.04	0.03	<0	*0.005	*0.003	*0.004	0.02	0.01	<0	<0	0.007	<0.0003
33	<0	0.03	0.06	<0	0.02	0.03	<0	*0.006	*0.005	*0.006	0.01	*0.006	<0	<0	0.005	<0.0002
34	<0	0.1	0.06	<0	0.04	0.05	*0.005	*0.008	*0.003	*0.003	<0	*0.004	<0	<0	0.005	<0.00009
35	<0	0.03	0.1	<0	0.02	0.02	<0	*0.006	<0.002	*0.003	0.02	0.05	0.05	0.6	0.004	<0.0004
36	<0	0.04	0.08	<0	0.02	0.02	*0.003	*0.005	<0.002	*0.004	0.01	0.04	0.05	<0	0.004	<0.0002
37	<0	0.05	0.08	<0	0.04	0.04	*0.005	*0.005	*0.004	*0.005	0.01	0.04	0.05	*0.006	0.004	*0.0006
38	<0	0.08	0.07	<0	0.05	0.05	*0.005	*0.006	*0.003	*0.004	0.01	0.03	0.05	<0	0.003	<0.0002
39	<0	*0.02	0.06	<0	0.02	0.02	*0.003	*0.004	<0.002	*0.003	*0.003	0.04	0.05	<0	0.003	<0
40	<0	<0	0.08	<0	0.01	0.01	<0	*0.002	<0.002	<0.0005	<0	0.01	0.06	<0	<0	<0
41	<0	<0	0.09	<0	0.03	0.03	*0.005	*0.005	*0.005	0.01	0.06	0.05	0.08	<0	0.007	<0.000006
42	<0	<0	0.06	*0.005	0.01	0.01	<0.002	*0.003	<0.002	*0.003	*0.003	0.03	0.06	<0	0.002	<0.00005
43	<0	0.6	0.08	<0	0.03	0.04	*0.005	*0.007	*0.007	*0.004	0.01	0.04	0.04	0.1	<0	<0
44	<0	<0	0.07	*0.004	0.03	0.03	*0.003	*0.003	<0.002	*0.004	*0.007	0.04	0.06	0.03	<0	<0.00002
45	<0	1.5	0.1	<0	0.06	0.06	*0.005	*0.007	0.009	0.03	0.1	0.08	0.1	<0	<0	<0
46	0.9	<0	0.1	<0	0.03	0.04	*0.005	*0.006	*0.004	*0.005	<0	<0	<0	<0	<0	
47	<0	<0	0.07	*0.007	0.04	0.05	*0.005	*0.006	*0.004	*0.005	0.009	0.04	0.04	<0	0.004	<0.0002

<: values below detection limit.
*: Values between LOD and LOQ.

Table S6. PFSA concentrations (ng g^{-1}) in each sample

Sample ID	PFBS	PFPeS	PFHxS	PFHpS	PFOS	PFOS br	PFNS	PFDS	9ClPF3O UdS	11ClPF3O UdS	4:2 FTS	6:2 FTS	8:2 FTS	10:2 FTS
1	0.04	<0	<0	<0	0.02	<0	<0	<0	<0	<0	<0	0.01	<0	*0.003
2	0.04	<0	<0	<0	<0	<0	<0	<0	<0.00005	<0	<0	0.02	<0	*0.003
3	0.03	<0	0.03	*0.003	<0	<0	<0	<0	<0.00003	<0	<0	0.02	<0	*0.003
4	0.03	<0	0.01	<0	0.04	0.04	<0	<0	<0.00006	<0	<0	0.02	<0.004	*0.005
5	*0.008	<0	<0	<0	<0	<0	<0	<0	<0	<0	<0	0.01	<0	<0.002
6	0.02	<0	0.02	<0	0.02	<0	<0	<0	<0.00004	<0	<0	0.01	<0	<0.002
7	0.01	<0	0.6	<0	<0	0.2	<0	<0	<0	<0	<0	0.04	<0.004	*0.004
8	0.01	<0	0.01	<0	0.02	0.03	<0	<0	<0.00002	<0	<0	0.03	<0.003	*0.003
9	0.03	<0	<0	<0	0.1	0.1	0.04	<0	<0.0006	<0.0005	<0	0.03	*0.02	0.02
10	0.02	<0	*0.006	<0	0.02	0.02	0.01	*0.007	<0.0002	<0.003	<0	0.02	<0.003	*0.006
11	0.009	<0	0.1	<0	0.04	0.04	*0.003	*0.007	<0.0005	<0.005	<0	0.03	<0.002	*0.006
12	0.04	<0	0.03	<0	0.03	0.03	<0	*0.004	<0.0001	<0.0003	<0	0.02	<0.001	*0.003
13	0.04	<0	1.2	<0	0.03	0.03	<0.002	*0.007	<0.0002	<0.002	<0	0.03	<0.002	*0.004
14	0.02	<0	*0.006	<0	0.02	0.0175	<0.002	*0.003	<0.0001	<0.002	<0	0.02	<0.003	*0.006
15	0.05	<0	*0.004	<0	0.01	0.01	<0.00002	<0	<0	<0	<0	0.01	<0.001	<0.001
16	0.2	*0.006	0.02	<0.001	0.05	0.05	<0.00005	<0	<0.0004	<0	<0	0.01	<0.003	*0.003
17	0.1	*0.004	0.02	<0.001	0.02	0.02	*0.003	*0.007	<0.0005	*0.006	<0	0.01	<0.004	0.01
18	0.1	0.02	0.02	<0	0.02	<0	<0	<0	<0	<0	<0	0.02	*0.007	*0.005
19	0.0523	<0	*0.006	<0	0.03	0.03	<0.0002	<0	<0.000008	<0	<0	0.01	<0.003	*0.007
20	0.09	<0	0.01	<0	0.04	0.04	<0	<0	<0	<0	<0	0.03	*0.006	<0.0006
21	0.1	<0	0.02	<0	0.03	0.03	<0	<0	<0.00003	<0	<0	0.03	*0.008	*0.004
22	0.08	<0	0.03	<0	0.03	0.02	<0	<0	<0.0001	<0	<0	0.02	<0.005	*0.006
23	0.2	*0.006	0.07	*0.003	0.05	0.05	*0.007	<0	<0.0006	<0	<0	0.02	<0.003	<0.002

24	0.1	<0	0.05	<0	0.2	0.2	<0	<0	<0.0001	<0	<0	0.03	0.06	0.04
25	0.2	0.01	0.06	<0	0.04	0.04	<0.0002	<0	<0.0001	<0.002	<0	0.02	*0.007	0.01
26	0.08	<0	0.1	<0	0.5	0.5	<0	*0.003	<0.002	<0	<0	0.06	0.1	0.06
27	0.03	<0	0.1	<0	0.9	0.9	<0	<0	<0	<0	<0	0.02	<0	<0
28	0.1	0.01	0.3	<0	0.9	0.9	<0	<0	<0	<0	<0	0.02	<0.003	<0.002
29	0.2	0.009	0.7	0.01	2	2	<0.00003	<0	<0.004	<0	<0	0.04	*0.008	<0.0008
30	0.1	<0	0.4	<0	0.5	0.5	<0	<0	<0.0002	<0	<0	0.03	*0.007	<0
31	0.1	<0	0.03	<0	0.06	0.07	<0	*0.003	<0	<0.0003	<0	0.03	<0.005	*0.006
32	0.08	<0	0.02	<0	0.04	0.04	<0.0007	*0.003	<0	<0.001	<0	0.04	<0.003	*0.005
33	0.09	<0	0.2	<0	0.04	0.04	<0.0006	*0.003	<0.00002	<0.001	<0	0.03	<0.004	*0.006
34	0.06	<0	0.02	<0	0.03	0.03	0.01	*0.003	<0	<0	<0	0.1	<0.005	*0.004
35	0.1	<0	0.5	0.03	0.06	<0	<0	<0	<0	<0.0002	<0	0.03	<0.002	*0.003
36	0.08	<0	0.09	0.01	0.04	0.04	<0	<0	<0	<0.0002	<0	0.02	<0.001	<0.002
37	0.05	<0	1.4	0.02	0.04	0.04	<0	*0.006	<0.00008	<0.002	<0	0.03	<0.003	*0.004
38	0.03	<0	1.3	0.02	0.03	0.03	<0.0006	<0	<0.0003	<0.0005	<0	0.07	<0.003	*0.003
39	0.05	<0	0.2	*0.007	0.02	0.02	<0	<0	<0.00004	<0.0006	<0	0.01	<0.001	<0.002
40	0.01	<0	0.01	<0	0.01	0.01	<0	<0.001	<0.00003	<0	0.04	0.01	<0.001	<0.001
41	0.06	<0	0.01	<0	0.02	0.02	<0.0002	<0.002	<0	<0.0007	<0	0.09	<0.004	*0.005
42	0.02	<0	*0.007	<0	*0.006	*0.006	<0.0001	<0.0009	<0.00001	<0.0004	<0	0.01	<0.002	<0.002
43	<0	<0	0.009	<0	0.01	0.02	<0	<0	<0	<0	<0	0.02	<0.003	*0.003
44	0.02	<0	0.009	<0	0.01	0.01	<0.0005	*0.002	<0.000007	<0.0008	<0	0.02	<0.001	<0.002
45	0.05	<0	0.04	<0	0.05	0.05	<0	<0	<0	<0.0004	<0	0.04	<0.005	*0.006
46	0.03	<0	0.01	<0	0.04	0.1	<0	<0	<0	<0	<0	0.03	<0.003	*0.003
47	0.05	<0.002	0.01	<0.0008	0.03	0.03	<0.0003	<0.002	<0.0002	<0.00004	<0	0.02	<0.004	*0.005

<: values below detection limit.
*: Values between LOD and LOQ.

Table S7. Individual concentrations of remaining PFAS (ng g^{-1}) in each sample

Sample ID	PFOSA	N-MeFOSA	N-MeFOSAA	N-EtFOSA	N-EtFOSAA	4:2 mPAP	6:2 mPAP	8:2 mPAP	6:2/6:2 diPAP	8:2/8:2 diPAP
1	<0	<0	<0	<0	<0	0.09	<0	0.01	0.03	0.1
2	<0	<0	<0	<0	*0.004	0.7	<0.0002	0.09	0.09	0.4
3	<0	<0	<0	<0	<0.002	0.08	<0	0.1	0.03	0.2
4	<0	<0	<0	<0	<0.002	0.2	<0.0004	0.4	0.04	0.2
5	<0	<0	<0	<0	<0.001	<0	<0	0.08	0.02	0.40
6	<0	<0	<0	<0	<0	<0	<0	<0	0.01	0.05
7	<0	<0	<0	<0	<0	42.7	<0	<0	0.1	<0
8	<0.0008	<0	<0.0007	*0.006	*0.003	*0.03	<0	<0	0.03	0.15
9	<0.002	<0	*0.005	<0	0.0647	0.43	<0	<0	0.6	4.6
10	<0.0003	<0	<0.0007	<0	*0.004	*0.02	<0	<0	0.3	<0
11	<0	<0	<0	<0	*0.003	0.2	<0	0.2	0.03	<0
12	<0	<0	<0.0003	<0	<0.002	0.05	0.02	0.7	0.08	<0
13	<0	<0	<0	<0	<0.002	0.2	<0	1.1	0.02	<0
14	<0.0005	<0	<0.002	<0	<0.002	*0.02	<0	0.15	0.04	<0
15	<0	<0	<0.0002	<0	<0.0009	0.06	*0.008	0.2	0.01	<0
16	<0	<0	<0.0003	<0	<0.002	0.05	<0	0.4	0.02	<0
17	<0	<0	<0.002	<0.002	*0.005	0.04	<0.0004	<0	0.02	0.4
18	<0	<0	<0	<0	<0	4.8	<0	<0	1.9	287
19	<0	<0	<0	<0	<0.002	0.3	0.02	<0	0.1	0.4
20	<0	<0	<0.0004	<0	<0.001	0.5	*0.005	2.7	0.03	<0
21	<0	<0	<0.0003	<0	<0.002	0.4	0.02	0.6	0.07	0.2
22	<0	0.2173	<0	<0	*0.003	0.1	<0	<0	0.07	0.3
23	<0	<0	<0	<0.001	<0.001	0.1	0.02	0.8	0.02	0.1

24	<0	<0	*0.004	<0	0.07	1.2	<0	<0	0.9	7.2
25	<0	<0	<0	<0	<0.001	3.3	0.7	<0	0.05	139.3
26	<0	<0	0.01	<0	0.1	0.2	<0	<0	0.7	8.9
27	<0	<0	<0	<0	<0	0.7	*0.006	0.01	0.09	32.6
28	<0	<0	<0	<0	<0	2.9	<0	0.9	0.08	86.4
29	<0	<0	<0	<0	*0.008	1.4	0.7	0.3	0.1	84.3
30	<0	<0	<0	<0	<0	11.5	<0	<0	0.06	240.6
31	<0	<0	<0	<0	<0	0.2	*0.007	0.3	0.08	0.1
32	<0.0003	<0	<0	<0	<0.0005	0.06	<0	0.06	0.05	0.2
33	<0	<0	<0	<0	<0.001	0.2	<0	0.06	0.04	0.04
34	<0	<0	<0	<0	<0	1.7	0.03	0.5	0.08	0.1
35	<0	<0	<0	<0	<0.001	0.2	<0	*0.002	0.01	0.09
36	<0.0009	<0	<0	<0	<0.001	0.1	*0.003	0.008	0.02	0.05
37	<0	<0	<0	<0	*0.003	0.1	<0	0.1	0.06	0.2
38	<0	<0	<0.001	<0	*0.003	0.1	<0	0.08	0.05	0.2
39	<0.002	<0	<0	<0	<0.002	0.09	<0.0007	0.5	0.02	0.06
40	<0	<0	<0.0006	<0	<0.002	<0	<0	<0	0.01	0.05
41	<0	<0	<0.001	<0	<0.002	0.2	<0	0.6	0.04	0.6
42	<0.0004	<0	<0.0007	<0	<0.002	*0.01	<0.002	0.2	0.02	0.07
43	<0	<0	<0.0003	<0	*0.004	*0.01	*0.007	0.5	0.03	0.2
44	<0.0001	<0	<0.0004	<0	<0.002	*0.02	0.01	0.09	0.02	0.2
45	<0.0003	<0	<0.0002	<0	*0.004	0.08	0.3	1.4	0.1	0.8
46	<0	<0	<0	<0	*0.003	0.3	<0	<0	0.2	11.7
47	<0.0001	<0	<0.0003	<0	*0.005	*0.02	0.04	0.2	0.06	0.4

<: values below detection limit.
*: Values between LOD and LOQ.

3.3. Correlations between target compounds.

Correlations between analytes were investigated taking into account all samples (See Table S8). Analysis was performed when analytes had a DF > 60%. Statistically significant positive correlations were found for half of the tests approximately ($0.3 < r < 0.8$, $p<0.05$), while statistically significant negative correlations were also found ($-0.3 < r < -0.5$, $p<0.05$) in 6 pairs of analytes (indicated in bold in Table S8).

Strong statistically significant positive correlations ($0.7 < r < 0.8$, $p<0.05$, indicated in dark grey) were found between some compounds of the PFCA group, such as PFNA and PFOA ($r=0.7$), which were also reported by other authors such as Sinclair and Kannan, (2006), van Driezum et al. (2014), Liu et al. (2019) and Pike et al. (2021). These correlations are high because the compounds are biodegradation products of the same precursors (Murakami et al., 2009). Other strong correlations were between PFTrDA and PFDoDA ($r= 0.7$) and with PFTeDA ($r= 0.8$), in agreement with Strynar and Lindstrom, (2008), who reported strong correlations between PFCAs at and > C9 PFCAs.

Strong correlations were also found between some PFCAs and compounds from the other groups, such as PFOA with 6:2/6:2 diPAP ($r= 0.7$) and with 8:2/8:2 diPAP ($r=0.7$). This is in accordance with a previous study of D'eon and Mabury (2007), who observed an increment of PFOA levels in the blood of rats exposed to 8:2/8:2 diPAP via oral ingestion, demonstrating biodegradation of PAPs in PFCAs since the first ones are less sterically hindered to be degraded by microbials compared to polymers (D'eon et al., 2009). This fact could maybe also explain the strong correlation between PFOA and 6:2/6:2 diPAP. Correlation between PFOS and PFOS Br was also found ($r= 0.8$).

Table S8. Spearman correlation values for each couple of PFAS in all samples. Highlighted values are statistically significant ($p<0.05$).

	PFHxA	PFOA	PFOA Br	PFNA	PFDA	PFDoDA	PFTrDA	PFTeDA	HFPO-DA
PFHxA	-								
PFOA	0.6	-							
PFOA Br	0.3	0.6	-						
PFNA	0.6	0.7	0.3	-					
PFDA	0.5	0.6	0.6	0.6	-				
PFDoDA	-0.07	-0.02	0.05	0.2	0.3	-			
PFTrDA	-0.2	-0.1	-0.08	-0.09	0.04	0.7	-		
PFTeDA	**-0.8**	-0.2	-0.2	-0.2	-0.09	0.5	0.8	-	
HFPO-DA	0.2	0.2	0.08	-0.006	0.2	-0.07	0.02	-0.1	-
PFBS	0.3	0.3	0.3	0.2	0.2	**-0.8**	-0.2	-0.3	0.4
PFHxS	0.07	0.2	0.3	-0.04	-0.02	-0.2	-0.1	-0.05	0.4
PFOS	0.3	0.4	0.4	0.4	0.3	-0.1	-0.02	-0.1	0.6
PFOS Br	0.23	0.4	0.4	0.4	0.2	-0.001	-0.1	-0.2	0.4
6:2FTS	0.1	0.4	0.5	0.2	0.3	0.2	0.2	0.2	0.2
10:2FTS	-0.1	0.2	0.4	0.1	0.4	0.6	0.5	0.2	0.1
4:2 mPAP	0.3	0.5	0.4	0.3	0.3	-0.2	**-0.8**	**-0.4**	0.5
6:2 mPAP	0.2	0.2	0.3	0.2	0.07	-0.2	-0.09	-0.04	0.3
8:2 mPAP	0.1	-0.1	-0.1	-0.02	-0.05	-0.2	-0.09	0.02	0.1
6:2/6:2 diPAP	0.3	0.7	0.5	0.4	0.4	0.3	0.1	-0.1	0.2
8:2/8:2 diPAP	0.4	0.7	0.3	0.5	0.4	0.08	0.004	-0.002	0.3

Strong correlations ($0.7 < r < 0.8$) are indicated in dark grey, moderately correlations ($0.5 < r < 0.6$) in median grey and slightly correlations ($0.3 < r < 0.4$) in slightly grey.

Table S8. (Continuation)

	PFBS	PFHxS	PFOS	PFOS Br	6:2FTS	10:2FTS	4:2 mPAP	6:2 mPAP	8:2 mPAP	6:2/6:2 diPAP	8:2/8:2 diPAP
PFBS	-										
PFHxS	0.4	-									
PFOS	0.6	0.5	-								
PFOS Br	0.4	0.5	0.8	-							
6:2FTS	0.2	0.4	0.4	0.5	-						
10:2FTS	0.1	-0.02	0.2	0.2	0.3	-					
4:2 mPAP	0.5	0.4	0.5	0.6	0.5	0.2	-				
6:2 mPAP	0.3	-0.01	0.2	0.2	0.1	-0.07	0.1	-			
8:2 mPAP	0.1	0.1	0.08	0.07	0.2	**-0.8**	-0.06	0.4	-		
6:2/6:2 diPAP	0.2	0.09	0.4	0.5	0.4	0.5	0.6	0.1	-0.2	-	
8:2/8:2 diPAP	0.3	0.07	0.3	0.3	0.2	0.2	0.4	0.09	-0.2	0.6	-

Strong correlations (0.7 < r < 0.8) are indicated in dark grey, moderately correlations (0.5 < r < 0.6) in median grey and slightly correlations (0.3 < r < 0.4) in slightly grey.

This work contains several strengths but also has its limitations. The study provides information on a large group of PFAS in FCMs used in fast food restaurants from France, which might be indicative for FCMs in other European countries. Given the limited number of samples, this information is not representative for the entire country. The data should rather be seen as indicative. Sampling could have been done in a more precise way, avoiding any contact with food items.

4. Conclusions.

Several groups of PFAS were quantified in FCMs from fast-food restaurants from France. PFHxA, 6:2 FTS and 6:2/6:2 diPAP were found in all samples (DF= 100%). The PAPs group was the dominant group, except 6:2 mPAP, which had a low DF and low concentration. Only two analytes were not found in any sample (PFOSA and 9Cl-PF3ONS). Some strong correlations were found in agreement with the literature. Compared to other studies, concentrations were lower in the studied FCMs, but DFs were higher for some analytes. This indicates the ubiquity of these compounds in daily products, which may be a risk for human health when products packed in these materials are regularly consumed. The short-chain (<C6) PFAS concentrations were relatively low.

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Block II:

Combination of SUPRAS and ambient mass spectrometry and applications.

Chemosphere

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Supramolecular solvent-based microextraction probe for fast detection of bisphenols by ambient mass spectrometry

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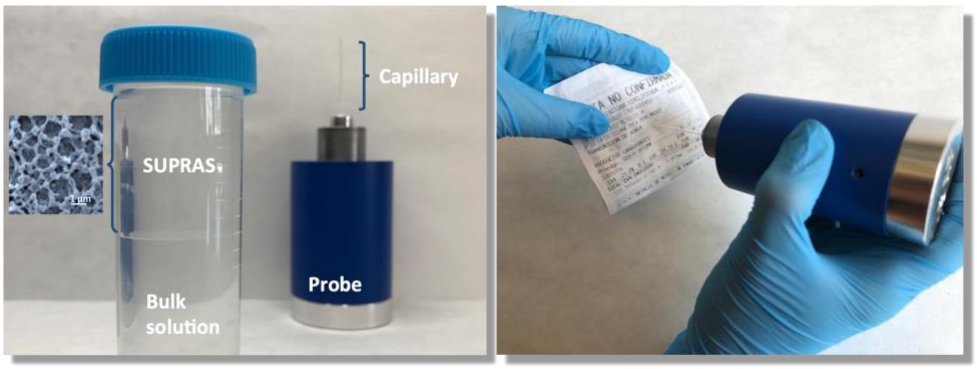


Highlights

- SUPRAS microextraction probes are proposed for fast detection of bisphenols by ASAP.
- Fast (10 s extraction, 1 min analysis) and simple (probe loading and sample contact).
- BPA and BPS were the most abundant in thermal paper.
- BPA is progressively being replaced by BPS in the Spanish market.

Abstract

In this study, we investigated for the first time the suitability of supramolecular solvent (SUPRAS)-based microextraction probe for the development of generic and fast sample treatment prior to qualitative analysis by ambient mass spectrometry (AMS) based on ASAP (atmospheric solids analysis probe). SUPRAS are nanostructured liquids formed by the self-assembly of amphiphilic aggregates with multiple binding sites and microenvironments of different polarity for the efficient extraction of multiple compounds at low volumes. Different types of SUPRAS were evaluated to improve the analytical features of ASAP (sensitivity, selectivity and reproducibility) and to reduce cross-contamination between analysis. All these aspects are crucial to extent the applicability of AMS to routine analysis. The method was applied to the screening of bisphenol A and structural analogues in thermal paper. Optimal results were achieved with SUPRAS synthesized with 1-decanol in mixtures of ethanol:water. SUPRAS (1.1-2 μL) were loaded onto glass probes and placed in contact with samples for 10 seconds before ASAP analysis. AMS signal peaks (width: 0.2-0.5 min) were easily integrated and normalized with internal standards (RSD: 2-25%). The method was applied to 62 samples of thermal paper. BPA and BPS were the most widely used, this highlighting the progressive industrial replacement of BPA by BPS.

Keywords: bisphenols; SUPRAS; ambient mass spectrometry; atmospheric solid analytical probe; thermal paper.

1. Introduction.

Ambient mass spectrometry (AMS) consists in modified atmospheric pressure ionization sources, where solid or liquid samples are directly introduced so that analytes desorb from the matrix and enter the MS detector. AMS diversified rapidly since first techniques appeared in 2004 (desorption electrospray ionization, DESI, by Takats et al. 2004) and 2005 (direct analysis in real time, DART, by Cody et al. 2005) giving rise to a variety of techniques, many times with 2D and 3D imaging possibilities (Awad et al. 2015, Laskin et al. 2016, Lu et al. 2018, Perez et al. 2019), and a variety of applications in very different fields, such as pharmaceutical, polymer, forensic, food and biological tissue analysis (Aszyk et al. 2018, Lu et al. 2018, Paine et al. 2014, Xiao et al. 2020).

The atmospheric-solids-analysis probe (ASAP) technique was first reported in 2005 by McEwen et al. In ASAP, the sample is loaded onto a disposable glass capillary which is placed against the hot stream of the nebulizer gas (N_2) and near the corona needle in an atmospheric pressure chemical ionization (APCI) source. Analytes are desorbed by high temperature and ionized trough the corona discharge reactions (McEwen, 2010). ASAP offers advantages over other AMS techniques, such as simplicity, speed and solvent-free operation (avoiding solubility limitations and the need of flow-rate optimization) (Blokland et al. 2020, Cechová et al. 2019, Cvijović et al. 2019, Gaiffe et al. 2018, McCullough et al. 2020, Wójtowicz et al. 2019).

The number of studies dealing with the development of sample preparation strategies coupled to AMS is increasing fast with the aim of improving the reproducibility, selectivity and sensitivity of these techniques. Modified electrospray tips (Deng et al. 2017a, Liu et al. 2019, Vasiljevic et al. 2019, Wong et al. 2013) and solid-phased microextraction (SPME) fibers or coated inlet probes (Gómez-Ríos and Pawliszyn, 2014, Wang et al. 2020, Zhao et al. 2019) have been proposed. The application of solvent-based approaches, mainly slug-flow microextraction (SFME), is

more limited but it is also gaining attention in the last years. In SFME, plugs of immiscible liquids (usually the extraction solvent and the liquid sample) are in contact in a thin capillary. Turbulences due to the movement of the plugs inside the thin probe ensure the mass transfer at the interface (Deng et al. 2017b, Ren et al. 2014, Zhang et al. 2019). SFME based on ethyl acetate was recently proposed for the analysis of polar compounds in biofluids with nanoESI-AMS. A pipette was used to force the movement of the liquid plugs and enhance recoveries (Zhang et al. 2019). In the same context, a multi-phase system based on two cationic ionic liquids (ILs) and a dichloromethane (DCM) layer was employed for the determination of perfluorinated compounds in waters. The sample was sandwiched between two ILs and the DCM phase, which was less viscous and allowed direct analysis by sonic-spray ionization (Lv et al.2019).

In this study, we investigated the suitability of supramolecular solvent (SUPRAS)-based microextraction probe for ASAP screening of organic contaminants in solid materials in a single step. SUPRAS are nanostructured liquids produced by self-assembly and coacervation of amphiphiles in aqueous or hydro-organic media. SUPRAS have a high number of available binding sites (amphiphile concentration ~0.1-1 mg/µL) and high surface area due to their discontinuous character what is beneficial for the efficient extraction of compounds at low volumes and under short extraction times. SUPRAS are also suitable for wide screening purposes and the obtainment of MS fingerprints since they offer regions of different polarity within their aggregates and they can stablish mixed interactions for the extraction of organic compounds (polar, ionic or hydrogen bonds with the polar groups of amphiphiles and the aqueous pools and dispersive interactions with the hydrocarbon chains layers). They also feature certain restricted access properties for clean-up and have been proven to exclude protein and polysaccharides in extraction processes (Ballesteros-Gómez and Rubio, 2012). These properties, together with their high surface tension and low volatility (that facilitate their confinement inside the glass capillary during extraction) and their low toxicity, make them excellent candidates for the proposed microextraction

probe format which is operated under simple contact with the sample for few seconds.

As proof-of-principle, the developed SUPRAS-based microextraction probes in combination with ASAP-MS/MS were applied to the screening bisphenol A and six replacements in thermal paper. BPA replacements were 4,4'-Sulfonyldiphenol (bisphenol S, BPS), 4,4´-Methylenediphenol (bisphenol F, BPF), 4-(4-phenylmethoxyphenyl)sulfonylphenol (BPS-MAE), 4-(4-propan-2-yloxyphenyl)sulfonylphenol (D-8), 4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (TGSA) and N-(p-Toluenesulfonyl)-N'-(3-p-toluenesulfonyl-oxyphenyl)urea Pergafast 201. SUPRAS made up of inverse aggregates of simple alcohols, diols and carboxylic acids prepared in THF:water or ethanol:water mixtures (Ballesteros-Gómez and Rubio, 2012, González-Rubio et al., Ruiz et al. 2007) were investigated in terms of compatibility, sensitivity and reproducibility with ASAP-MS/MS analysis of target compounds. The optimal method was applied to the analysis of 62 samples of thermal paper in order to investigate the extent of the recent BPA replacement in the Spanish market.

2. Material and methods.

2.1. Chemicals and reagents.

Solvents were methanol (MeOH), ethanol and tetrahydrofuran (THF), obtained from VWR – Prolabo Chemicals (Bois, France). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain). 1-hexanol, 1-decanol (98%), 1-tetradecanol, 1,2-decanediol (98%) and 1-decanoic acid (98%) were from Sigma–Aldrich Co. (St. Louis, USA) and hydrochloric acid (37%) was supplied by Merck (Darmstadt, Germany).

Internal standards (IS) Bisphenol A-d_{16} (BPA-d_{16}) and bis(4-hydroxyphenyl) Sulfone-d_8 (BPS-d_8) were acquired from Toronto Research Chemicals (Toronto, Canada). Stock solutions of IS (BPS-d_8 and BPA-d_{16}) were prepared in MeOH (5 mg·mL^{-1}) and stored at -20ºC. Intermediate and working solutions were prepared by appropriate dilution in MeOH and also stored at -20ºC. Table S1 shows the full names, CAS numbers, molecular formula and physical-chemical properties of the target compounds.

2.2. Apparatus.

Determination of BPA and replacements was carried out using an Agilent Technologies 6420 Triple Quadrupole mass spectrometer equipped with an atmospheric pressure chemical ionization (APCI) source modified with ASAP unit (Ionsense Inc., see Figure S1). The source was operated in negative mode. Optimal source parameters recommended for ASAP were: gas temperature, 325°C; gas flow, 4.0 L·min^{-1}; vaporization temperature, 400ºC, nebulizer gas pressure, 20 psi; capillary voltage, -1000 V; Corona voltage, 10 µA. After the probe was inserted in the ASAP unit, the MS signal was recorded for 1 min.

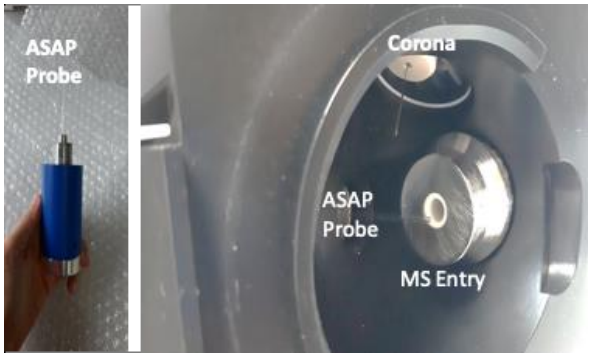
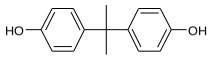
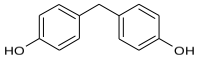
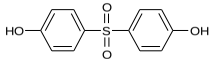
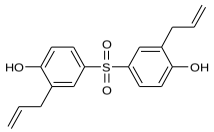
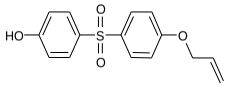
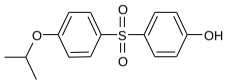
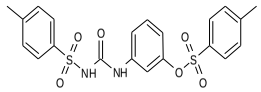


Figure S1. *ASAP probe and APCI source used in this study*

Qualitative analysis MassHunter workstation software from Agilent Technologies was used for determination of bisphenols, registering characteristics transitions for each analyte (see Table S2, according to Dueñas-Mas et al. 2019).

Table S1. Target compounds (physical chemical properties correspond to measured data unless other stated)

Chemical structure	Abbreviation	CAS	Formula	Molecular weight	[a]Water solutiblity ($mg \cdot L^{-1}$)	[b]logK_{ow}	[c]pK_a	[d]Vapor pressure (mm Hg)
	BPA	80-05-7	$C_{15}H_{16}O_2$	228.29	120-300	3.32	9.59-11.30	$3.99x10^{-8}$
	BPF	620-92-8	$C_{13}H_{12}O_2$	200.24	190 (estimated)	2.91	7.55	$3.7x10^{-7}$ (Estimated)
	BPS	80-09-1	$C_{12}H_{10}O_4S$	250.27	1,100	1.2	8	$<1x10^{-8}$ (Estimated)
	TGSA	41481-66-7	$C_{18}H_{18}O_4S$	330.40	4.79	3.22	8.3-8.5	$9.5x10^{-10}$
	BPS-MAE	97042-18-7	$C_{15}H_{14}O_4S$	290.34	83 (estimated)	3.1 (estimated)	8.2 (estimated)	$<1x10^{-8}$ (Estimated)
	D-8	95235-30-6	$C_{15}H_{16}O_4S$	292.35	21	3.36	8.2	$<1x10^{-8}$ (Estimated)
	Pergafast 201	232938-43-1	$C_{21}H_{20}N_2O_6S_2$	460.50	35	2.6	12.5; 5.3; -3.8; -13.6 (estimated)	$<1x10^{-8}$ (Estimated)

Abbreviations: BPA, Bisphenol A; BPF, Bisphenol F; BPS, Bisphenol S; TGSA, 4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol ; BPS-MAE, 4-(4-phenylmethoxyphenyl)sulfonylphenol ; D-8, 4-(4-propan-2-yloxyphenyl)sulfonylphenol ; Pergafast 201, N-(p-Toluenesulfonyl)-N'-(3-p-toluenesulfonyl-oxyphenyl)urea.

[a-d]https://www.epa.gov/sites/production/files/2014-05/documents/bpa_final.pdf

Table S2. MRM transitions, dwell time, fragmentor voltage and collision energy. Quantifiers for target compounds are indicated in bold.

Compounds	Precursor Ion (m/z)	Product Ion (m/z)	Dwell time (ms)	Fragmentor (V)	Collision energy (eV)
BPA	**227.1**	**212.2**	**50**	**100**	**20**
BPA	227.1	113.0	50	100	24
BPF	**199.0**	**105.0**	**50**	**100**	**25**
BPF	199.0	93.0	50	100	30
BPS	**249.0**	**108.0**	**50**	**100**	**20**
BPS	249.0	92.1	50	100	32
BPS-MAE	**289.1**	**248.1**	**50**	**100**	**20**
BPS-MAE	289.1	184.1	50	100	30
D8	**291.1**	**248.0**	**50**	**100**	**25**
D8	291.1	184.1	50	100	25
TGSA	**329.1**	**132.1**	**50**	**100**	**25**
TGSA	329.1	148.1	50	100	25
Pergafast	**459.1**	**170.0**	**50**	**100**	**30**
Pergafast	459.1	262.1	50	100	25
BPA-d_{16}	**241.2**	**223.0**	**50**	**100**	**20**
BPA-d_{16}	241.2	141.9	50	100	30
BPS-d_8	**257.3**	**112**	**50**	**100**	**25**
BPS-d_8	257.3	96	50	100	25

BPA-d_{16} was used to correct BPA and BPS-d_8 to correct the rest of compounds.

Glass melting point capillaries (0.8-1.1 i.d., 90 mm length) were obtained from Pyrex (Thermo Fisher Scientific, USA). For optimization experiments and SUPRAS production we employed a vortex-shaker REAX Top (Heidolph, Schwabach, Germany) equipped with a head (ref. 549-01000-00) with 10 microtubes from Heidolph (Schwabach, Alemania) and a 36 x 2.2/1.5 mL angle rotor (ref. 1162) MPW350R high speed centrifuge from MPW Med-Instruments (Warschaw, Polonia).

2.3. SUPRAS sample treatment optimization.

SUPRAS were synthesized from ternary solutions of 50 mL containing the amphiphile (5% v/v), organic solvent (10-30% v/v) and water (65-85%). Various amphiphiles (1-hexanol, 1-decanol, 1-tetradecanol, 1,2-decanediol and 1-decanoic acid) and two organic solvents (THF and ethanol) were tested. Milli-Q water was employed as coacervating agent (poor solvent for the amphiphile) and was acidified at pH ~2.5 for SUPRAS made up of 1-decanoic acid in order to ensure the protonated form of amphiphile, which is needed for SUPRAS formation. Synthetic solutions were vortex-stirred for 5 min and centrifuged for 5 min at 2.500 rpm to accelerate phase separation. The upper SUPRAS phase was transferred to a closed glass bottle and stored at 4°C until used (within 1 week).

Tickets containing BPA, BPS, Pergafast 201 and TGSA were used as representative samples for optimization (due to the limited amount of material and to prevent contamination after manipulation of the samples, different tickets were used for different batches of experiments along the optimization process). The selection of this type of samples was done on the basis that thermal paper allowed to easily obtain homogeneous samples in enough quantity for optimization. SUPRAS composition was first optimized by carrying out the sample treatment in 2 mL Eppendorf microtubes by simple contact of SUPRAS phase (400 µL, ISs 1 mg/L) with the sample aliquots (20 mg) during 1 h without stirring. Extraction experiments were done in triplicate. Glass probes were then immersed (open end) into the SUPRAS phase and immediately analysed (n=5) by ASAP-MS/MS. SUPRAS volume loaded on the open side of the probe was calculated by weight difference before and after probe loading and ranged from 1.1 to 2 µL. Solid samples were also directly analysed by scratching the surface of the paper sample with the open end of the probe so that solid particles (few milligrams) remained on it (Ballesteros-Gómez et al. 2014). Statistical comparisons were performed with Minitab software Ver. 18 (Minitab Inc, State College, Pennsylvania, USA) using one-way analysis of variance (ANOVA) and Tukey's tests (p-value < 0.05).

2.4 SUPRAS-based microextraction probe-ASAP-MS/MS optimal method for analysis of BPA and replacements in thermal paper.

SUPRAS of inverse aggregates of 1-decanol were prepared from 50 mL of 5% v/v amphiphile, 10% ethanol and 85% water. The open end of a disposable glass probe was immersed in SUPRAS (with 1 mg/L ISs) and loaded with 1.1-2 μL solvent. Then, the SUPRAS-based microextraction probe was carried out by immediately putting it in contact with the sample surface for 1-60 s. The position of the probe during extraction was horizontal and perpendicular to the sample. The probe was then injected in the ASAP unit for MS analysis. Experiments were done 5 times per sample. Blanks were injected between samples to ensure lack of cross-contamination.

2.5. Thermal paper samples.

Samples were collected in Córdoba (Spain) from October 2019 till January 2020. Thermal paper samples *(n*=62) were classified in four groups: food stores and restaurants (*n*=23), ATMs (*n*=7), petrol stations and public transport (*n*=10) and other stores (clothes, cosmetics, stationer's, etc., *n*=22).

3. Results and discussion.

3.1. SUPRAS composition optimization.

SUPRAS formation occurs in two consecutive stages. First, tridimensional aggregates (micelles or vesicles, generally) are spontaneously formed by self-assembly of amphiphilic compounds when they reach a critical micellar/vesicular concentration. Then, these aggregates increase their size and/or are reorganized by the action of the

coacervate agent (pH or temperature change, or addition of a salt or a poor solvent for the amphiphile) so that a new liquid phase (SUPRAS) is formed and separated from the bulk solution. This new phase presents a complex internal nano- or microstructure, such as bilayers, inverse hexagonal phase, sponge phase, etc. (Romera-García and Ballesteros-Gómez, 2020). Figure 1 shows the formation process of SUPRAS of inverse aggregates in organic solvent by the addition of water (poor solvent for the amphiphile, coacervating agent). They have been successfully employed in the extraction of a wide variety of organic contaminants in liquid and solid samples (Ballesteros-Gómez and Rubio, 2012, including bisphenols and analogues in biological samples (Romera-García et al. 2019), wastewater (Ruiz et al. 2008) and indoor dust (Dueñas-Mas et al. 2019).

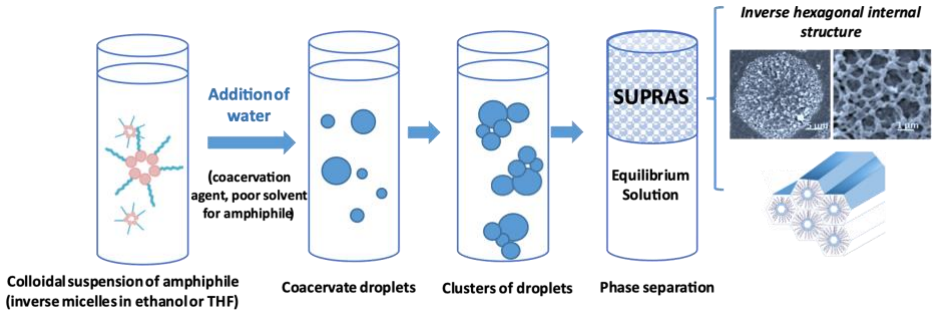


***Figure 1**. Schematic picture of the SUPRAS formation and its expected microstructure.*

First, we investigated the influence of the functional group of the amphiphile forming the SUPRAS on the suitability for ASAP-MS/MS analysis. SUPRAS were made up from solutions of 5% v/v of 1-decanol, 1,2-decanediol or 1-decanoic acid, 20% v/v of THF and 75% of milli-Q water (acidified in the case of 1-decanoic acid at pH ~2.5) and containing 1 mg/L of ISs. The MS peaks areas of the quantifier ions of each analyte and of ISs were recorded and results were expressed as absolute areas or as relative areas ($area_{analyte}/area_{IS}$).

Results with SUPRAS made up of 1-decanol were similar to those synthesized with the diol (in terms of sensibility and reproducibility). The ratio $area_{1\text{-decanol}}/area_{1,2\text{-decanediol}}$ (absolute areas) of BPS, BPA, Pergafast and TGSA were 0.8, 1.2, 1.3 y 1.6, respectively. These values seem to be related with the higher amount of water in SUPRAS of 1,2-decanediol (~30% w/w) with regard to that of SUPRAS of 1-decanol (~5% w/w) under the same synthesis conditions (Ballesteros-Gómez and Rubio, 2012, González-Rubio et al.). So, the lower the water solubility of the compounds (TGSA<Pergafast<BPA<BPS, see table S1) the better they were extracted with 1-decanol-based SUPRAS. Due to the fact that all the analytes were better extracted with 1-decanol-based SUPRAS (except the most water soluble compound, BPS) this was selected as optimal. Furthermore, SUPRAS formation diagrams were wider for 1-decanol than for 1,2-decanediol (Ballesteros-Gómez and Rubio, 2012, González-Rubio et al.), thus allowing the synthesis of SUPRAS in a wider composition range. SUPRAS of 1-decanoic acid were discarded due to strong matrix suppression effects.

After selection of SUPRAS based on simple alcohols, we investigated the influence of the amphiphile alkyl chain length. SUPRAS constituted by 1-hexanol, 1-decanol and 1-tetradecanol were compared. The solid sample was also directly measured in order to verify that the sample preparation step with SUPRAS was beneficial.

The MS signal as a function of time was clearly different with and without SUPRAS treatment. MS signals from SUPRAS-based microextraction probe-ASAP-MS/MS resulted in signal peaks of 0.2-0.4 min, which could be easily integrated for data processing. Contrarily, the direct injection of solid samples did not show a clear peaks and MS signals kept almost constant during several minutes before starting to gradually drop. As an example, Figure 2 shows the registered MS signal (BPA quantifier) of a representative sample with (2A) and without (2B) SUPRAS treatment.

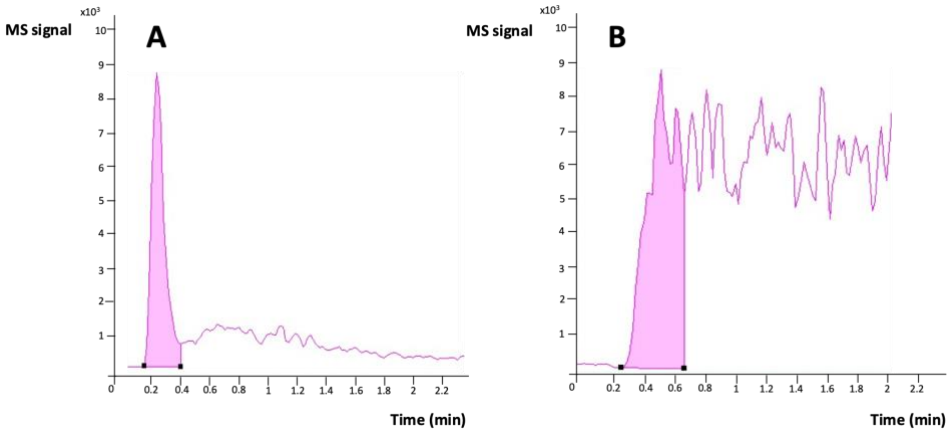


Figure 2*. Absolute AMS peak areas of BPA (quantitative transition) in a thermal paper sample analysed by (A) previous extraction with SUPRAS of 1-decanol (1 h) (SUPRAS synthesis mix composition: 5% v/v amphiphile, 75% v/v water and 20% THF v/v) and (B) direct analysis of the solid.*

Other advantage of the use of SUPRAS treatment was that during the direct analysis of solids, particles were easily released from the probe and deposited onto the APCI source, thus generating cross-contamination and the need of cleaning the source between injections. With the direct analysis of the solid, values of relative standard deviation (RSD, %) were very high (50-90%), most probably due to variations in the loaded volume on the probe and the lack of correction by ISs. Furthermore, the signal from the less volatile compounds (TGSA and Pergafast 201, see vapor pressure values in Table S1) were considerably lower (around 2-4 times) than those observed from SUPRAS treated samples (results not shown). By adding ISs to SUPRAS, variations due to differences in probe loading (and instrument fluctuations) could be corrected down to 25% RSD, values that can be considered acceptable for screening purposes.

When comparing the performance of SUPRAS constituted by 1-hexanol, 1-decanol and 1-tetradecanol (relative AMS peak areas) we could observe that the extraction efficiency of the target compounds slightly improved with the lower chain length, as shown in Figure 3 (differences were only significant among the three alkanols for Pergafast 201 and for BPS with 1-tetradecanol). This was not due to differences in the ionization

process since average absolute areas of ISs did not change significantly among the different SUPRAS treatments. In contrast, RSDs slightly improved with the higher chain length and values were 4-25% with 1-hexanol, 2-16% with 1-decanol and 3-14% with 1-tetradecanol. The SUPRAS synthesized with 1-decanol was selected as an optimal compromise between sensibility and reproducibility.

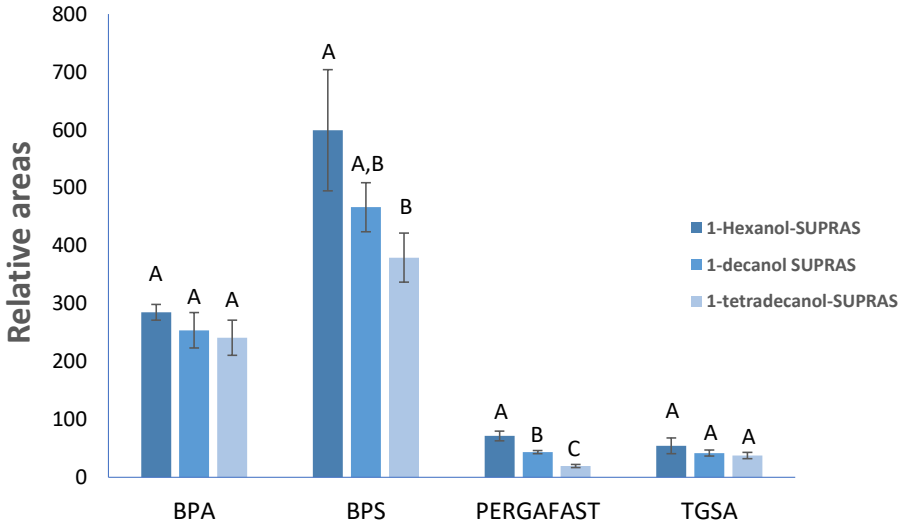


Figure 3. *Relative AMS peak areas of BPA, BPS, Pergafast 201 and TGSA in thermal paper samples analysed after 1 h extraction with SUPRAS made up of 1-hexanol, 1-decanol and 1-tetradecanol (SUPRAS synthesis mix composition: 5% v/v amphiphile, 75% v/v water and 20% THF v/v). Significant differences are indicated by different letters on the top of the bars (Tukey tests).*

SUPRAS of 1-decanol were then synthesized in different organic solvent:water mixtures. THF and ethanol at 10, 20 and 30% v/v were investigated for the synthesis of SUPRAS. Table S3 shows solubility and volatility parameters of THF, ethanol and water for discussion. SUPRAS of inverse aggregates are formed in mixtures of water and a wide variety of protic and aprotic organic solvents (Romera-García and Ballesteros-Gómez, 2020). THF:water has been the most employed synthesis solvent mixture.

Table S3. Dielectric constant, Teas fractional solubility parameters (derived from Hildebrand solubility parameters), dielectric constant, volatility and boiling point of synthesis solvents.

	Dielectric constant (ε)	Teas fractional solubility parameters			(Vapor pressure, 20°C)	Boiling point
		F_d (Dispersion component)	F_p (Polar component)	F_h (Hydrogen bonds component)		
Water	80.1	21	22	57	17.5 mm Hg	100 °C
Ethanol	24	36	18	46	43.9 mm Hg	78 °C
THF	7.5	55	19	26	132 mm Hg	66° C

Due to the low dielectric constant and predominance of dispersive binding forces, THF enhances the extraction of non-polar compounds. When it is mixed with water (of high dielectric constant and predominance of hydrogen bonds binding forces) this results in mixtures of wide polarity and solubility that favor SUPRAS formation in a wider range of composition. We also investigated the use of ethanol:water mixtures. Ethanol as a protic and more polar solvent, provided a more balanced contribution of dispersion, polar and hydrogen bonds forces to improve the extraction of polar and moderately polar compounds. Furthermore, it is less volatile and toxic than THF.

Figure 4 shows results with SUPRAS made up of 1-decanol and different solvent mixtures at 10, 20 and 30% v/v. Relative AMS peak areas for BPA, BPS and Pergafast 201 generally decreased with the THF percentage while the opposite trend was observed for TGSA. Contrarily and with the exception of BPS and Pergafast 201, relative AMS peak areas increased with the ethanol percentage. Since not an optimal solvent and solvent percentage values could be found for all the compounds, we selected 10% v/v ethanol for further experiments on the basis of toxicity and minimal solvent consumption. Additionally, lower percentages of organic solvent in the synthesis should result in SUPRAS of higher viscosity, cohesive forces and lower volatility because of the higher content in amphiphile and lower content in organic solvent (Ballesteros-Gómez and Rubio, 2012). These properties are beneficial to maintain SUPRAS structure and volume onto the glass capillary during the extraction. In this

way, analytes diffuse from the sample to the SUPRAS phase contained in the probe and the loss of SUPRAS soaking the sample is minimized (as it would occur with conventional solvents) thus being available for ASAP injection.

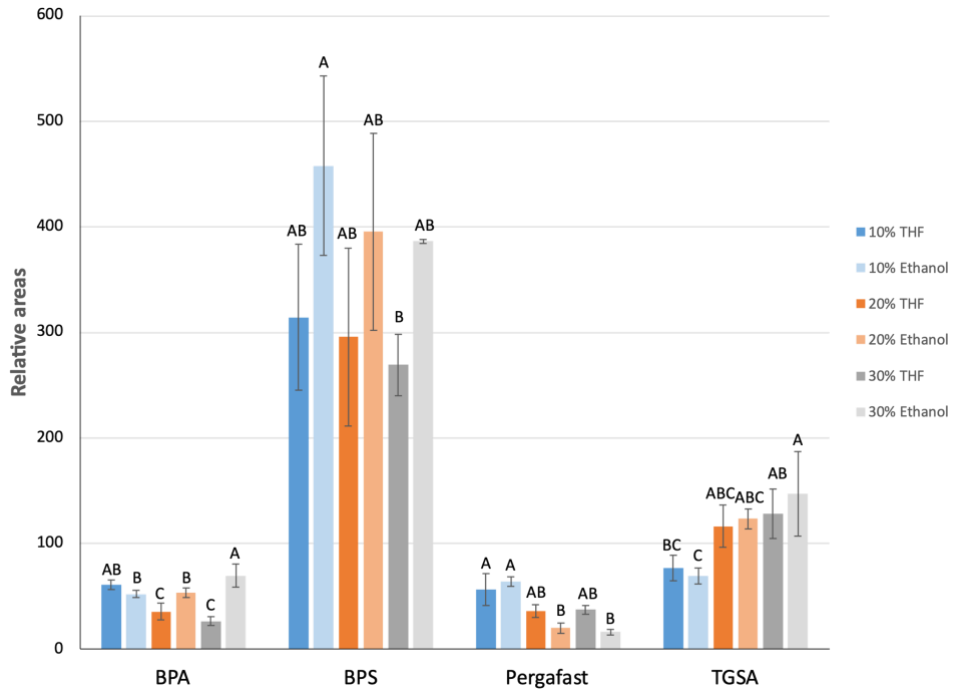


***Figure 4**. Relative AMS peak areas of BPA, BPS, Pergafast 201 and TGSA in thermal paper samples analysed after 1h extraction with SUPRAS made up of 1-decanol and different synthesis percentages of THF or ethanol (SUPRAS synthesis mix composition: 5% v/v amphiphile, 65-85% v/v water and 10-30% organic solvent v/v). Significant differences are indicated by different letters on the top of the bars (Tukey tests).*

3.2. SUPRAS-based microextraction probe optimization.

Finally, we investigated the feasibility of the SUPRAS-based microextraction probe approach coupled to ASAP-MS/MS. For this purpose, SUPRAS synthesized with 5% v/v of 1-decanol, 10% v/v of ethanol and 85% of water were tested.

SUPRAS (1.1-2 μL) were loaded inside probes (open end) by simple immersion. The open end of glass probes containing SUPRAS were placed in contact with the sample surface for 1-60 s. The probe was placed in horizontal position and perpendicular to the sample. An extraction time of 10 seconds was proposed as optimal. Longer extraction times led to significant losses of SUPRAS by adsorption onto the sample, while shorter times originated irreproducible results. At this time period, ISs areas kept similar when compared with the extraction performed in Eppendorf tubes during 1 h contact this suggesting that the most of the SUPRAS volume remained in the glass capillary and that there were not significant losses during the extraction process. Relative AMS peak areas (see figure S2) neither dropped drastically when using the SUPRAS loaded probes (1.3, 1.1, 1.4 and 2.3 times lower for BPA, TGSA, Pergafast 201 and BPS). This suggests a fast mass transfer process approaching equilibrium after 10 s and similar SUPRAS/sample ratios in both extraction procedures. It must be noted that the ratio SUPRAS volume/sample was similar in both cases with values of 20 mL/g sample for extractions performed in Eppendorf tubes and in the range ~24-43 mL/g sample for the SUPRAS probe approach (considering the approximate i.d. of the probe as 1 mm to estimate the extracted sample aliquot and the mean sample weight as 5.9 mg/cm^2).

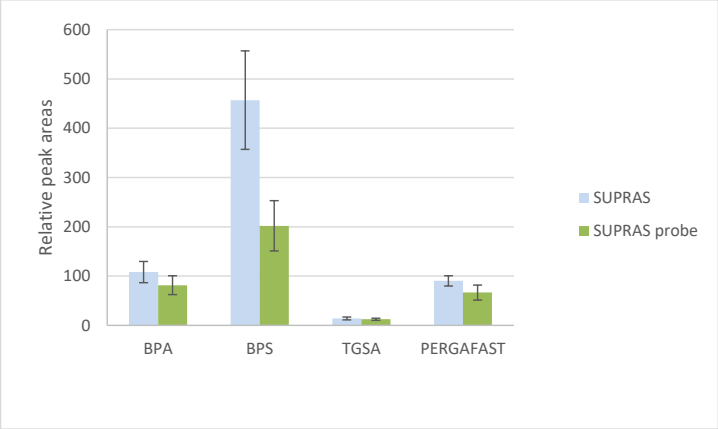


Figure S2. *ASAP-MS/MS signal from 4 thermal paper samples ($area_{analyte}/area_{IS}$) after extraction with SUPRAS loaded probes (contact time 10 s) and SUPRAS extraction in Eppendorf tubes (contact time 1 h).*

3.3. Analysis of thermal paper samples.

Optimal SUPRAS (synthesized with 5% v/v of 1-decanol, 10% v/v of ethanol and 85% of water) were applied for the microextraction probe-ASAP-MS/MS analysis of 62 samples of thermal paper collected in Córdoba (Spain). Table 1 shows the screening results (presence of major and secondary compounds).

Table 1. Bisphenols found in thermal paper samples.

	Sample	Major bisphenol	Secondary bisphenols with lower abundance
Shops (clothes, cosmetics, libraries, etc.)	1	BPS	
	2	BPS	BPA
	3	BPS	
	4	BPA	BPS
	5	BPS	
	6	BPA	BPS
	7	BPS	BPA
	8	BPA	BPS
	9	BPS	Pergafast, BPA
	10	BPS	D-8
	11	BPA	BPS
	12	BPA	BPS
	13	BPS	BPA
	14	BPS	BPA, D-8
	15	BPS	BPA, D-8
	16	BPA	BPS
	17	BPA	BPS
	18	BPS	BPA
	19	BPS	BPA, D-8
	20	BPA	BPS
	21	BPS	BPA, D-8
	22	TGSA	BPS, BPA
Supermarket and restaurants	1	Pergafast	BPS, BPA
	2	BPS	D-8
	3	BPA	
	4	BPS	D-8
	5	BPA	
	6	BPA	
	7	BPA	
	8	BPS	

	9	BPA	
	10	BPS	
	11	BPA	
	12	BPS	
	13	BPS	D-8
	14	BPA	BPS
	15	BPA	BPS
	16	BPA	BPS
	17	BPS	D-8
	18	BPS	BPA
	19	BPS	BPS, D-8
	20	BPA	
	21	BPS	BPA
	22	BPA	BPS
	23	BPS	BPA
Transports and gas stations	1	BPS	BPA
	2	BPA	BPS, D-8
	3	BPA	BPS
	4	BPA	BPS
	5	BPS	BPA, D-8
	6	BPS	
	7	BPS	
	8	BPS	
	9	BPS	
	10	BPS	BPA, D-8
Banks	1	BPS	BPA, D-8
	2	BPA	BPS
	3	BPS	D-8
	4	BPA	BPS
	5	BPA	BPS, D-8
	6	BPA	
	7	BPA	BPS

BPA (*n*=27), BPS (*n*=33), Pergafast 201 (*n*=1) and TGSA (*n*=1) were detected as major color developers in thermal paper samples. These results are slightly different from those found in previous studies in Europe or in Spain. Thus, Ververliet et al. 2019 (sample collection years 2017 and 2018) reported detection frequencies (DFs) of 67.6%, 15.1%, 12.6% and 0.84% for BPA, BPS, Pergafast 201 and TGSA, respectively, in European countries. Björnsdotter et al. 2017 (sample collection year 2016) revealed total DFs

of 55% BPA, 21% BPS and 21% Pergafast 201 in cash receipts from Europe while in Spain DFs were 88% BPA followed by 8% BPS. Molina-Molina et al. 2019 (sample collection year 2017) measured DFs of BPA and BPS in Spain, Brazil and France. While samples from Spain and Brazil showed a major use of BPA (DFs ≥ 90%) values in France were 51% for BPA and 21%, for BPS. In the present study (sample collection in late 2019 and early 2020), we found in Spain an increasing use of BPS (DF 53%) in detriment of BPA (DF 44%) with respect to these previous studies. This suggests that legislative restrictions and growing concern by adverse effects of BPA have led to replace BPA by BPS in the recent Spanish market. The use of the other studied substitutes (Pergafast 201 and TGSA) remains still minor in Spain with DFs similar to those reported by Vervliet et al. 2019. However, Pergafast 201 have been found at higher DF in other European countries, e.g. a value of 14% was reported in the Netherlands (Björnsdotter et al. 2017). Similarly, Eckardt et al. 2017 reported DFs for Pergafast 201 of 36% in 2017, 34% in 2018 and 49.5% in 2019 in thermal papers from Germany.

Together with the main developer we detected the co-ocurrence of secondary or trace developers in many samples. BPS was detected at low abundance in 19 of 27 samples with BPA as main developer. Similarly, some samples containing BPS as major color developer contained low abundance peaks of BPA (8 out of 33), of both BPA and D-8 (7 out of 33) or of BPA and Pergafast 201 (one sample). D-8 was in total detected in 16 samples and always as secondary compound. Finally, also the samples containing TGSA and Pergafast 201 contained trace levels of BPA and BPS.

These results are in agreement with previous studies where the simultaneous presence of several bisphenols in the same thermal paper samples has been described. Secondary color developers at trace levels have been frequently found in thermal paper and may be due to cross-contamination during manufacturing or to the use of recycled paper (Björnsdotter et al. 2017, Verveliet et al. 2019, Yang et al.2019).

Furthermore, these secondary compounds have been also reported at higher relative abundance than just trace levels in some samples and this may be explained by the use of industrial mixtures (Björnsdotter et al. 2017, Verveliet et al. 2019, Yang et al. 2019). As an example, Verveliet et al. 2019 found these mixtures in 42 of the 308 samples, being D-8 the most frequently used secondary color developer in Europe.

3. Conclusions.

A rapid and simple sample preparation strategy based on SUPRAS-based microextraction probes for screening of BPA and replacements in materials prior to ASAP analysis is proposed. SUPRAS made up of inverse aggregates of 1-decanol in ethanol:water mixtures (containing 1 mg/L ISs) were loaded in ASAP glass probes (1.1-2 μL) and extraction was made by simple contact with the sample surface during 10 seconds. Subsequent ASAP-MS/MS analysis (1 min) generated MS peaks that could be processes as reproducible and integrable signals after IS correction (0.2-0.4 min peaks, areas RSD of 2-25%). Contrarily, the direct analysis of solids generated a continuous MS signal and common cross-contamination due to the release of particles inside the MS source. Samples of thermal paper from South Spain were screened. Results suggested that BPA has been quickly replaced by BPS, while the use of other alternatives (TGSA, Pergafast 201, D-8, etc.) is still limited.

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Declaration of competing interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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Supramolecular solvent extraction and ambient mass spectrometry for the determination of organic contaminants in food packaging material

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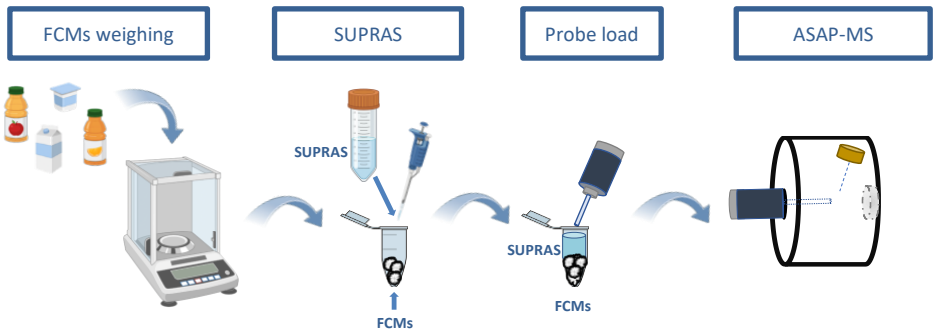


Highlights

SUPRASs and ambient mass spectrometry were combined for fast analysis.

Quantification (bisphenols and aryl-OPFRs) and screening were performed in FCMs.

Bisphenols (n.d.-292 μg·g^{-1}) and aryl-OPFRs (n.d.-14.2 μg·g^{-1}) were present in samples.

Other 14 additives and unknown compounds were identified in FCMs too.

Abstract

A rapid method based on a fast sample treatment with supramolecular solvents (SUPRASs) and ambient mass spectrometry (AMS) analysis was developed for the screening and quantification of organic contaminants in food packaging materials (FCMs). The suitability of SUPRASs made up of medium chain alcohols in ethanol:water mixtures was investigated, given their low toxicity, proven capacity for multi-residue analysis (since they provide a wide variety of interactions and multiple binding sites) and restricted access properties for simultaneous sample extraction and clean-up. Two families of emerging organic pollutants, bisphenols and organophosphate flame retardants, were targeted as representative compounds. The methodology was applied to 40 FCMs. Target compounds were quantitated using ASAP (atmospheric solids analysis probe)-low resolution MS and a broad-spectrum screening of contaminants was performed through spectral library search using direct injection probe (DIP) and high resolution MS (HRMS). The results showed the ubiquity of bisphenols and of some flame retardants, as well as the presence of other additives and unknown compounds in about half of the analyzed samples, which highlight the complex composition of FCMs and the possible associated health risks.

Keywords: bisphenols; flame retardants; supramolecular solvents; ambient mass spectrometry; ASAP; DIP

1. Introduction.

The chemical safety of food contact materials (FCMs) remains a priority for the European Food Safety Authority (EFSA) since there are still significant gaps and regulatory challenges (Muncke et al. 2017, 2014; Simoneau et al. 2016). While around 8,000 substances are regulated in FCMs, the so-called non-intentionally added substances (NIAS) are mostly unregulated. NIAS are impurities, by-products or degradation products, which are originated during the processing or the recycling of materials and that could constitute the majority of chemicals present in a product (Grob, 2014).

There is a growing concern about the presence of hazardous contaminants in FCMs. Recent studies have confirmed the presence of poly and per-fluorinated compounds, phthalates, bisphenol A and nonylphenol in pizza boxes (Rosenmai et al. 2017), contaminants related to printing inks in different food containers (Lago and Ackerman, 2016) and brominated flame retardants in thermal cup lids (Turner and Filella, 2017). In order to ensure safer FCMs, the complex chemical cocktail present in these materials needs to be elucidated. However, most of the current analytical methods are hampered by multiple, laborious and slow solvent extraction and clean-up steps that target certain groups of contaminants (Bignardi et al. 2014; Giannetti et al. 2017; Sanchis et al. 2017). To prevent these drawbacks, analysis should be matrix- and compound- independent, so that emerging and potentially toxic compounds are not overlooked. Methods need to be also rapid in order to provide consumers, the industry and institutions with fast answers to take immediate action.

In this study we combine a fast sample treatment step, which is based on supramolecular solvent extraction, with a fast analysis technique [atmospheric solids analysis probe and direct injection probe (ASAP-MS and DIP-MS)] coupled to with low and high resolution mass spectrometry to determine organic contaminants in FCMs. The first one was used to

quantify the target compounds, while the last one was used to perform a broad-spectrum screening of contaminants through spectral library search. In ASAP-MS and DIP-MS, solid or liquid samples or extracts are loaded onto a disposable glass capillary and directly introduced onto an atmospheric chemical pressure ionization (APCI) source. Analytes are desorbed from the matrix by high temperature and ionized trough the corona discharge reactions and enter the detector (McEwen et al. 2005). The only difference between the two AMS sources, which were those provided by each MS system manufacturer, was the position of probe inside the source with respect to the MS entrance. In ASAP-MS this position is opposite and in DIP-MS is orthogonal.

Supramolecular solvents (SUPRASs) are nanostructured liquids produced from amphiphilic compounds in aqueous or hydro-organic media through self-assembly and coacervation processes (Figure 1).

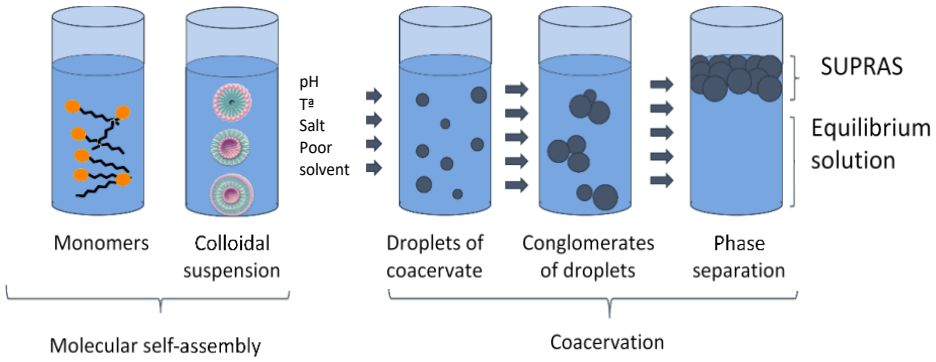


Figure 1. *SUPRAS formation by self-assembly and coacervation.*

They are a great option to replace conventional organic solvents in analytical extractions due to their physico-chemical properties. These properties include: (a) mixed interaction mechanisms with organic compounds (e.g. polar, ionic, hydrogen, dispersion interactions, etc.), (b) presence of regions with a wide range of polarity in the supramolecular aggregates, (c) high number of available binding sites (high concentration of amphiphile in the range 0.1-1 mg·μL^{-1}), (d) behavior as restricted access materials for polar macromolecular interferents and (e) low volatility and toxicity in comparison with conventional solvents. (Ballesteros-Gómez and Rubio, 2012; Ballesteros-Gómez et al. 2010). SUPRASs have been used with excellent results in analytical extractions of a wide variety of organic compounds in liquid and solid biological, food and environmental samples (Ballesteros-Gómez and Rubio, 2012; Ballesteros-Gómez et al. 2010; Dueñas-Mas et al. 2019; Romera-García et al. 2019; Ruiz et al. 2007).

The application of SUPRASs to materials has been more limited. Recently, we developed a fast qualitative screening method for the analysis of BPA and analogs with SUPRASs loaded into ASAP probes, which were put in contact with thermal paper samples for few seconds before ASAP analysis by using low resolution MS/MS (Dueñas-Mas et al. 2022). In the present study, we apply the SUPRAS treatment in a separate step that is simple and fast, in order to make quantitative analysis easier. Two families of widely spread emerging organic compounds, i.e. bisphenols and analogs and aryl-organophosphate flame retardants (aryl-OPFRs), were investigated and quantitatively determined in FCMs. Among materials, plastics were selected as representative since they are one of the most frequently used FCMs (Simoneau et al. 2016). Furthermore, the SUPRAS-DIP technique was evaluated to carry out a broad-spectrum screening analysis using high resolution MS/MS and library search based on the wide variety of interactions supplied by SUPRASs.

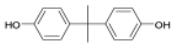
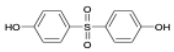
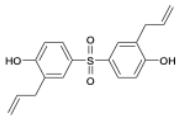
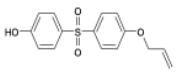
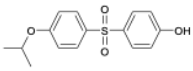
2. Experimental section.

2.1. Chemicals and reagents.

Methanol (MeOH) and ethanol (EtOH) were supplied by Fisher Scientific (Madrid, Spain). Ultra-high-quality water was obtained from a Milli-Q water purification system (Millipore, Madrid, Spain). 1-hexanol and 1-decanol were acquired from Sigma-Aldrich (Steinheim, Germany). The target aryl-OPFRs were bisphenol A bis(diphenyl phosphate) (BDP, CAS 5945-33-5), cresyl diphenyl phosphate (CDP, CAS 26444-49-5), 2-ethylhexyl diphenyl phosphate (EHDPP, CAS 1241-94-7), isodecyl diphenyl phosphate (IDPP, CAS 29761-21-5), resorcinol bis(diphenyl phosphate) (RDP, CAS 57583-54-7) and triphenyl phosphate (TPHP, CAS 115-86-6). All of them were obtained from AccuStandard (New Haven, CT) as 1 mL ampoules (~100 μg·mL-1 of analyte certified concentration in toluene), except TPHP and the internal standard (IS) TPHP-d_{15}, which were acquired as solids from Sigma Aldrich (Zwijndrecht, the Netherlands). Bisphenols were 4,4'-(propane-2,2-diyl) diphenol (bisphenol A, BPA) and 4,4'-Sulfonyldiphenol (bisphenol S, BPS), obtained from Sigma-Aldrich (St. Louis, MO, USA), and 4-(4-phenylmethoxyphenyl)sulfonylphenol (BPS-MAE), 4-(4-propan-2-yloxyphenyl) sulfonylphenol (D-8) and 4-(4-hydroxy-3-prop-2-enylphenyl)sulfonyl-2-prop-2-enylphenol (TGSA), which were acquired from Toronto Research Chemicals (Toronto, Canada), together with the internal standards BPA-^{13}C12 y BPS-d_8. See Tables S1 and S2 in supporting information for more details about structures and physico-chemical properties of target compounds.

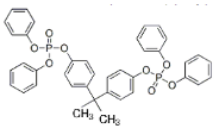
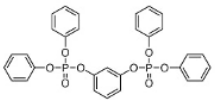
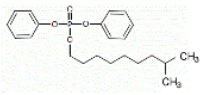
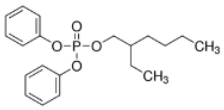
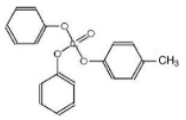
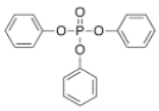
Spike solutions of ISs (one for aryl-OPFRs with TPHP-d_{15}, and one for bisphenols with a mix of BPA-^{13}C12 and BPS-d_8) were prepared in MeOH at concentrations of individual compounds of 5 mg·L^{-1}, for both optimization and sample analysis. Stock and working solutions of bisphenols and aryl-OPFRs were prepared by dilution in MeOH. All solutions were stored at -20ºC.

Table S1. Molecular structure, compound name, CAS number, chemical formula, molecular weight, water solubility, log Kow and pKa of BPA and analogs.

Chemical structure	Abbreviation	CAS	Formula	Molecular weight	Water solubility (mg L^{-1})	$logK_{ow}$	pK_a
	BPA	80-05-7	$C_{15}H_{16}O_2$	228.29	120-300	3.32	9.59-11.30
	BPS	80-09-1	$C_{12}H_{10}O_4S$	250.27	1,100	1.2	8
	TGSA	41481-66-7	$C_{18}H_{18}O_4S$	330.40	4.79	3.22	8.3-8.5
	BPS-MAE	97042-18-7	$C_{15}H_{14}O_4S$	290.34	83	3.1	8.2
	D-8	95235-30-6	$C_{15}H_{16}O_4S$	292.35	21	3	8.2

Abbreviations: BPA, Bisphenol A; BPF, Bisphenol F; BPS, Bisphenol S; TGSA, Bis-(3-allyl-4-hydroxyphenyl) sulphone; BPS-MAE, Phenol,4-[[4-(2-propen-1- yloxy)phenyl]sulfonyl; D-8, 4-Hydroxyphenyl 4-isoprooxyphenylsulphone.

Table S2. Molecular structure, compound name, CAS number, chemical formula, molecular weight, water solubility, log Kow and pKa of aryl-OPFRs.

Chemical structure	Abbreviation	CAS	Formula	Molecular weight	Water solubility (mg L^{-1})	logKow
	BDP	5945-33-5	$C_{39}H_{34}O_8P_2$	692.6	---	10.8[a]
	RDP	57583-54-7	$C_{30}H_{24}O_8P_2$	574.5	---	7.6[a]
	IDPP	29761-21-5	$C_{22}H_{31}O_4P$	390.5	0.75 mg/L	5.44
	EHDPP	1241-94-7	$C_{20}H_{27}O_4P$	362.4	1.9 mg/L	5.730
	CDP	26444-49-5	$C_{19}H_{17}O_4P$	340.3	Insoluble	5.25
	TPHP	115-86-6	$C_{18}H_{15}O_4P$	326.3	1.9 mg/L	4.59

Abbreviations: BDP, Bisphenol A-bis (diphenyl phosphate); RDP,Resorcinol bis(diphenyl phosphate); IDPP, Isodecyl diphenyl phosphate ; EHDPP, 2-ethylhexyl diphenyl phosphate ; CDP, Cresyl Diphenyl Phosphate; TPHP, Triphenyl phosphate; [a]calculated values.

2.2. Apparatus.

Instrumentation for SUPRAS preparation and extraction of FCMs were a vortex-shaker REAX Top (Heidolph, Schwabach, Germany) equipped with a head (ref. 549-01000-00) with 10 microtubes from Heidolph (Schwabach, Germany) and a 36 x 2.2/1.5 mL angle rotor (ref.

1162) MPW350R high speed centrifuge from MPW Med-Instruments (Warschaw, Poland).

2.3. SUPRAS preparation.

On the basis of our previous study (Dueñas-Mas et al. 2022), SUPRASs were made up from solutions containing the amphiphile (either 1-hexanol or 1-decanol, 5% v/v), ethanol (10%, v/v) and water (85%, v/v). Mixtures were stirred for 5 min for extraction and centrifuged for 5 min at 2,500 rpm to accelerate the phase separation. Approximately, a volume of ~39 µl of SUPRAS/ml of initial synthesis solution were formed under these conditions. Once both phases were separated, the upper phase (SUPRAS) was transferred to a closed glass bottle and stored at 4°C until use (within 1 week).

2.4. Collection and analysis of FCMs.

A total of 40 samples from different types of FCMs were acquired from local supermarkets (Córdoba, Spain). They were mainly plastic materials (see Table S3). FCMs were thoroughly rinsed with distilled water before analysis. Sample extraction was carried out in 2 mL microtubes which contained 20 mg of samples cut in small pieces (~0.1 x 0.1 cm) and 400 µL of SUPRAS (10 mg·g^{-1} IS). They were vortex-shaken for 5 min and centrifuged for 5 min at 10,000 rpm. Then, the open end of a disposable glass probe was immersed in the SUPRAS extract and it was loaded with 1-2 µL of SUPRAS. The probe was immediately injected in the ASAP or DIP unit for MS analysis (n=5). Samples were extracted in triplicate. Blanks of MeOH were injected between samples to ensure lack of cross-contamination.

Table S3. Type of packaging, material (plastic type) and contained food

Type of package	Main material	Food
1. **Cup**	Plastic	Yogurt
2. **Cup lid**	Plastic with aluminum coating	Yogurt
3. **Cup**	Plastic	Yogurt
4. **Cup**	Plastic	Yogurt
5. **Cup**	Plastic (6)	Yogurt
6. **Cup**	Plastic (4)	Yogurt
7. **Cup**	Plastic (5)	Cheese
8. **Cup lid**	Plastic	Cheese
9. **Cup**	Plastic (5)	Cheese
10. **Bottle**	Plastic with aluminum coating (3)	Milk
11. **Bottle cap**	Plastic (2)	Milk
12. **Bottle**	Plastic with aluminum coating (2)	Soup
13. **Cap**	Plastic (2)	Soup
14. **Bag**	Plastic	Grated cheese
15. **Bag**	Plastic	Bread
16. **Bag**	Plastic	Potatoes
17. **Capsule**	Plastic	Coffee
18. **Capsule lid**	Plastic	Coffee
19. **Bag**	Paper	Tea
20. **Bag**	Plastic with aluminum coating	Seeds
21. **Bag**	Plastic	Chickpeas
22. **Bag**	Plastic with aluminum coating	Pate
23. **Container**	Plastic	Donuts
24. **Container lid**	Plastic	Donuts
25. **Tub**	Plastic	Apple cream
26. **Tub lid**	Plastic	Apple cream
27. **Bag**	Plastic with aluminum coating	Isotonic drink
28. **Bag**	Plastic	Gum
29. **Bag**	Plastic with aluminum coating	Soup
30. **Cup**	Plastic	Yogurt
31. **Bottle**	Plastic (2)	Liquid yogurt
32. **Bottle lid**	Plastic (4)	Liquid yogurt
33. **Cup**	Cardboard	Coffee
34. **Cup lid**	Plastic (6)	Coffee
35. **Bag**	Plastic with aluminum coating	Protein bar
36. **Lid**	Plastic with aluminum coating	Cheese
37. **Wrap**	Plastic	Cheese
38. **Pan**	Aluminum	Lasagna pan
39. **Bag**	Plastic with aluminum coating	Seeds
40. **Container**	Plastic	Burgers

Identification code of the type of plastic when available: 2: HDPE (Polyethylene of high density); 3: PVC (Polyvinyl Chloride); 4: LDPE (Polyethylene of low density); 5: PP (Polypropylene); 6: PS (Polystyrene).

Quantitative determination of bisphenols and aryl-OPFRs in FCMs was performed using an Agilent Technologies 6420 Triple Quadrupole mass spectrometer equipped with an atmospheric pressure chemical ionization source (APCI) modified with an ASAP unit (Ionsense Inc.), which operated in positive mode for the analysis of aryl-OPFRs and in negative mode for bisphenols. Optimal source parameters for ASAP were: gas temperature, 325°C; gas flow, 4.0 $L \cdot min^{-1}$; vaporization temperature, 400ºC, nebulizer gas pressure, 20 psi; capillary voltage, +4500V (positive mode) and -1000 V (negative mode); corona voltage, 4 µA (positive mode) and 10 µA (negative mode). After the probe was inserted in the ASAP unit, the MS signal was recorded for 1 min. Probes were disposable glass melting point capillaries (0.8-1.1 i.d., 90 mm length) and were obtained from Pyrex (Thermo Fisher Scientific, USA). Qualitative analysis MassHunter workstation software from Agilent Technologies was used for data analysis. Characteristics MRM transitions were registered for each analyte (see Tables S4 and S5).

Table S4. Monitored MS/MS transitions for bisphenol A and its derivatives and detection parameters (APCI -)

Compounds	Precursor ion (m/z)	Product Ion (m/z)	Fragmentor (V)	Collision energy (eV)
BPA	**227.1**	**212.2**	**100**	**20**
BPA	227.1	113.0	100	24
BPS	**249.0**	**108.0**	**100**	**20**
BPS	249.0	92.1	100	32
BPS-MAE	**289.1**	**248.1**	**100**	**20**
BPS-MAE	289.1	184.1	100	30
D8	**291.1**	**248.0**	**100**	**25**
D8	291.1	184.1	100	25
TGSA	**329.1**	**132.1**	**100**	**25**
TGSA	329.1	148.1	100	25
BPA-^{13}C12	**239.2**	**223.0**	**100**	**20**
BPA-^{13}C12	239.2	141.9	100	30
BPS-d_8	**257.3**	**112**	**100**	**25**
BPS-d_8	257.3	96	100	25

Table S5. Monitored MS/MS transitions for aryl-OPFRs and detection parameters (APCI +)

Compounds	Precursor ion (m/z)	Product Ion (m/z)	Fragmentor (V)	Collision energy (eV)
BDP	**693.2**	**367.2**	**156**	**47**
BDP	693.2	115.2	156	101
CDP	**341.1**	**65.2**	**116**	**89**
CDP	341.1	91.2	116	53
EHDPP	**363.1**	**251.1**	**71**	**11**
EHDPP	363.1	77.1	71	93
IDPP	**391.2**	**251.1**	**81**	**15**
IDPP	391.2	77.1	81	73
RDP	**575.1**	**77.2**	**151**	**115**
RDP	575.1	152.2	151	79
TPHP	**327.1**	**77.1**	**150**	**40**
TPHP	327.1	215	135	30
TPHP-d_{15}	**342.2**	**82.2**	**150**	**135**
TPHP-d_{15}	342.2	222.1	150	135

Broad spectrum screening with library search was carried out with a high-resolution mass spectrometer (Bruker TimsTOF, Q-TOF) equipped with an APCI source with an unit for direct sample injection probe (DIP). Parameters of APCI source were: end plate offset, 500V; capillary voltage, 2500 V; corona voltage, 3000 nA; nebulizer gas pressure, 2.5 bars; dry gas, 3 $L \cdot min^{-1}$; dry temperature, 200 °C; vaporizer temperature, 350°C. Data acquisition was achieved in auto-MS/MS mode (abundant ions isolation and fragmentation) in order to perform a search on an open access spectral library (https://massbank.eu/MassBank/,MassBank_NIST.msp). The data acquisition programs were Data Analyst and Metaboscape (Bruker Daltonics). Identification was carried out on the basis of mass accuracy (<10 ppm), isotopic pattern fit expressed as mSigma (<200) and MS/MS score (>500). The calculation of the mSigma value is based on the relative

mean square of the difference of an experimental mass spectrum from the theoretical isotopic pattern of a specific molecular formula. The instrument includes a maximum mSigma threshold value of 200 for molecular formula assignment. Therefore, the lower the mSigma value, the more precise the fit. The MS/MS score describes the difference between the measured and the theoretical fragmentation spectrum of the measured ion. Score-based equations typically include the m/z-intensity pairs of the search spectrum and library spectra as well as additional parameters such as weighing functions. MS/MS scores range from 0 to 999. A low score indicates that the compound is not found in the database, and scores of 999 would present a perfect hit. The instrument sets a minimum threshold value for MS/MS score of 500.

3. Results and discussion.

3.1. Quantitation of bisphenols and aryl-OPFRs with SUPRAS-ASAP-QqQ-MS/MS.

Calibration curves for bisphenols and aryl-OPFRs (0.01-1 mg·L^{-1}, 0.5 mg·L^{-1} of IS) in SUPRAS of 1-hexanol and 1-decanol were analyzed by ASAP-QqQ-MS/MS. Determination coefficients were over 0.99. Differences between calibration slopes were compared by appropriate t-tests (Andrade et al. 2014). Results are showed in Table 1.

Table 1. Slopes ($L \cdot mg^{-1}$) and determination coefficients (R^2) of calibration curves of target compounds made in SUPRAS and analyzed by ASAP-QqQ-MS/MS. Instrumental detection (LOD, $\mu g \cdot L^{-1}$) and quantification (LOQ, $\mu g \cdot L^{-1}$) limits are provided for SUPRAS of 1-decanol (optimal). Method LODs and LOQs ($\mu g \cdot g^{-1}$) are provided in brackets.

	Bisphenols			Aryl-OPFRs	
	SUPRAS_C_6	**SUPRAS_C_{10}**		**SUPRAS_C_6**	**SUPRAS_C_{10}**
TGSA	3.4 ± 0.1 R^2=0.993	7.5 ± 0.3 R^2=0.992 LOD: 0.7 (*0.02*) LOQ: 2 (*0.06*)	**BDP**	0.37± 0.02 R^2=0.994	0.59 ± 0.03 R^2=0.993 LOD: 0.7 (*0.01*) LOQ: 2 (*0.04*)
D8	2.7 ± 0.12 R^2=0.988	7.4 ± 0.4 R^2=0.992 LOD: 1 (*0.03*) LOQ: 4 (*0.1*)	**RDP**	0.127 ± 0.003 R^2=0.9992	0.279± 0.007 R^2=0.997 LOD: 3 (*0.06*) LOQ: 10 (*0.2*)
BPS-MAE	4.9 ± 0.2 R^2=0.996	11.6 ± 0.6 R^2=0.990 LOD: 0.3 (*0.01*) LOQ: 1 (*0.03*)	**IDPP**	2.2 ± 0.04 R^2=0.9988 *t=0.16*	2.16 ± 0.07 R^2=0.998 LOD: 1 (*0.02*) LOQ: 3 (*0.06*)
BPS	4.7 ± 0.2 R^2= 0.996 *t=0.31*	4.6 ± 0.1 R^2=0.998 LOD: 3 (*0.1*) LOQ: 10 (*0.3*)	**EHDPP**	2.51 ± 0.04 R^2=0.9987 *t=1.04*	2.40 ± 0.09 R^2=0.993 LOD: 3 (*0.06*) LOQ: 10 (*0.2*)
BPA	1.28 ± 0.03 R^2= 0.998 *t=0.6*	1.24 ± 0.05 R^2=0.994 LOD: 17 (*0.4*) LOQ: 50 *(1.3)*	**CDP**	0.42 ± 0.02 R^2=0.9944 *t=1.26*	0.46 ± 0.02 R^2=0.995 LOD: 3 (*0.06*) LOQ: 10 (*0.2*)
			TPHP	10.3 ± 0.3 R^2=0.9956 *t =1.28*	10.9 ± 0.4 R^2=0.996 LOD: 0.7 (*0.01*) LOQ: 2 (*0.04*)

**Calculated t values are shown when they were lower than tabulated t values (meaning no significant differences between slopes with SUPRAS made up of C_6 and C_{10}).*

SUPRAS prepared with 1-decanol provided equal or better sensitivity than those with 1-hexanol and this was selected as optimal for further analysis. Slopes were 1-3.5 times higher for D8, TGSA, BPS-MAE,

RDP and BDP with SUPRAS of 1-decanol in ASAP, this showing the influence of the amphiphile on the ionization process of some analytes due to the lack of previous LC separation. Instrumental limits of detection (LODs) and quantification (LOQs) were in the ranges 1 - 20 $\mu g \cdot L^{-1}$ and 2 – 50 $\mu g \cdot L^{-1}$ for bisphenols, respectively, and 1 – 3 $\mu g \cdot L^{-1}$ and 2 – 10 $\mu g \cdot L^{-1}$ for aryl-OPFRs, respectively, and they were around one order of magnitude higher than those obtained with LC-ESI-QqQ-MS/MS and LC-APCI-QqQ-MS/MS, respectively (LODs: 0.06-1.2 $\mu g \cdot L^{-1}$ and LOQs: 0.12-2.4 $\mu g \cdot L^{-1}$ for bisphenols (Dueñas-Mas et al. 2019) and LODs: 0.03-0.7 $\mu g \cdot L^{-1}$ and LOQs: 0.07-1.4 $\mu g \cdot L^{-1}$ for aryl-OPFRs (Dueñas-Mas et al. 2020). The lower injection volume (1.1-2 µL in ASAP), different ionization source for bisphenols and the lack of LC separation leading to higher background noise are probable reasons.

Recoveries of internal standards in samples were acceptable and in the ranges 108 – 120% for TPHP-d_{15} (used for aryl-OPFRs), 75 – 120% for BPA-^{13}C12 (used for BPA) and 60 – 78% for BPS-d_8 (used for the rest of bisphenols). Method LODs and LOQs were estimated from instrumental values, considering an amount of sample of 0.02 g, 0.4 mL SUPRAS extract volume and the lowest IS recovery for each group of compounds. Taking into account this, the estimated method LODs (0.01-0.4 $\mu g \cdot g^{-1}$) and LOQs (0.04-1.3 $\mu g \cdot g^{-1}$) were low enough for the quantitative trace analysis of contaminants in materials (down to 0.001% considering the highest LOQ level).

Analysis of bisphenols and aryl-OPFRs in FCMs with SUPRAS-ASAP-QqQ-MS/MS.

Once SUPRAS of 1-decanol were selected as optimal, 40 samples from different FCMs (see Table S3) were analyzed and quantified following the specifications given in section 2.4. Target compounds were found in 18 samples (detection frequency, DF=45%). Results are shown in Table 2. All

Table 2. Levels of bisphenols and aryl-OPFRs found in food packaging samples (µg·g^{-1}). Only positive samples are shown.

Sample	TGSA	D8	BPS-MAE	BPS	BPA	EHDPP	CDP
1	n.d.	0.28 ± 0.02	0.17 ±0.01	1.6±0.2	<LOQ	<LOQ	**14.2±1.6**
3	n.d.	0.468±0.006	0.057±0.006	**21.4±1**	n.d.	n.d.	n.d.
7	n.d.	n.d.	0.052±0.00012	**n.d.**	n.d.	n.d.	n.d.
10	n.d.	0.28 ± 0.02	0.14±0.02	**10.4±0.2**	n.d.	n.d.	n.d.
11	n.d.	0.168±0.002	0.054±0.002	**292±28**	<LOQ	n.d.	n.d.
15	n.d.	0.30±0.06	0.0526±0.0006	7±1.4	2.2±0.4	n.d.	n.d.
18	n.d.	0.5±0.1	0.13±0.02	**16±5**	<LOQ	n.d.	n.d.
19	n.d.	0.316±0.06	0.064±0.008	**106±6**	<LOQ	n.d.	n.d.
20	n.d.	n.d.	n.d.	n.d.	n.d.	<LOQ	4.6±0.6
21	n.d.	0.38±0.06	<LOQ	**86±14**	n.d.	n.d.	n.d.
25	n.d.	n.d.	n.d.	n.d.	n.d.	0.20±0.04	4.4±1.2
26	n.d.	n.d.	n.d.	n.d.	n.d.	0.20±0.02	n.d.
33	n.d.	0.32±0.06	0.11±0.02	4.0±0.4	n.d.	n.d.	n.d.
36	n.d.	n.d.	<LOQ	<LOQ	n.d.	<LOQ	n.d.
37	1.8±0.2	1.3 ± 0.3	0.294±0.002	8.2±0.8	<LOQ	<LOQ	0.28±0.04
38	n.d.	2.44±0.08	0.09±0.02	**16±5**	1.26 ±0.06	<LOQ	1.2±0.08
39	n.d.	0.22±0.02	n.d.	0.5±0.1	n.d.	<LOQ	n.d.
40	n.d.	0.556± 0.08	0.24±0.01	**122±14**	<LOQ	<LOQ	n.d.
DF (%)/40 samples	2.5	32.5	35	35	20	22.5	12.5
Method LOD (µg·g^{-1})	0.02	0.03	0.01	0.1	0.4	0.06	0.06
Method LOQ (µg·g^{-1})	0.06	0.1	0.03	0.3	1.3	0.2	0.2

DF: detection frequency (%). Values > 10 µg·g^{-1} (0.001% p/p) are highlighted

positive samples were made up of plastic except sample 19 (paper tea bag), 33 (cardboard coffee cup) and 38 (aluminum lasagna pan). However, these materials, which are intended for warming up food or for containing hot food, have usually thermoplastic coatings, such as PVC, polypropylene or epoxy resins in contact with food. In fact, many food packages are not only formed by a single material, but they have several layers or sheets of different materials and mixtures. In Table S3, the nature of the main material of each FCM is given. For those items that were labelled by the manufacturer, the type of plastic is indicated too.

Results in Table 2 highlight the ubiquity of bisphenols in FCMs. BPA values (n.d.-2.2 $\mu g \cdot g^{-1}$, DF: 20%) were in a similar range or lower than those found in other studies (n.d.-3.09 $\mu g \cdot g^{-1}$ (Wang et al. 2019), n.d.-67.2 $\mu g \cdot g^{-1}$ (Chen et al. 2017) and n.d.-25.4 $\mu g \cdot g^{-1}$ (Pérez-Palacios et al. 2012). The two quantifiable levels of BPA were found in a plastic package of bread (unknown composition) and in an aluminum pan. BPA is employed in the synthesis of epoxy resins or internal food can linings and in polycarbonate bottles (EFSA CEF Panel 2015). It is also used as additive in other type of plastics, such as polysulphones, polyacrylates and PVC and it can be found in paintings, printing inks and thermal paper (Geens et al. 2012). As it was mentioned above, the presence of BPA in the aluminum pan was probably due to the fact that this item was protected with a thermoplastic coating.

BPS was the most frequently detected bisphenol (DF: 35%) and at higher concentrations (n.d.-292 $\mu g \cdot g^{-1}$). These results revealed the growing substitution of BPA by BPS, which has been proved by other authors (Chen et al. 2017, Vázquez-Loureiro et al. 2018). The greater concentration was found in a bottle cap made up of PET (polyethylene terephthalate). Although bisphenols are not traditionally associated to production of this type of plastic, a recent study has demonstrated their presence in recycled PET packages (Dreolin et al. 2019). Authors related the presence of bisphenols in PET with printing inks or other materials, or cross contamination during the processing. The presence of BPS in FCMs has

been scarcely investigated and only two studies provided concentrations ranges of n.d.-7.5 µg·g^{-1} (Chen et al. 2017) and n.d.-12.17 µg·g^{-1} (Vázquez-Loureiro et al. 2018). It should also be noted that the presence of the other analyzed BPA replacements, have been only studied in thermal paper so far (Björnsdotter et al. 2017, Eckardt et al. 2017). D8 and BPS-MAE were detected with similar frequencies (DF: 32.5-35%) than BPS, although at lower concentration levels in the ranges of n.d.-2.44 µg·g^{-1}and n.d.-0.29 µg·g^{-1}, respectively.

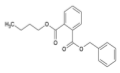
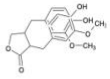
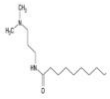
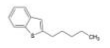
Aryl-OPFRs are plasticizers (among other functions). Their presence in food items have been reported in the last decade but scarcely in FCMs. To the best of knowledge, only a study of 2019 found 3 aryl-OPFRs, namely EHDPP (2-etilhexyl diphenyl phosphate), TCPP [tris (2-chloropropyl) phosphate] and TPHP (triphenyl phosphate) in tetrabricks and juice containers, although they were not quantified. Among them, only EHDPP is a permitted substance to be used in FCMs (Sanchis et al. 2019). As it can be seen in Table 2, EHDPP was found in the range n.d.-0.2 µg·g^{-1} (DF: 22.5%) and CDP was also present in five samples with levels ranging n.d.-14 µg·g^{-1}. EHDPP was quantified in two samples at the same concentration, which were a tube and its tube lid from the same package of apple cream, so that probably the same material was employed. The highest level of CDP was found in a yogurt cup, being the type of plastic of unknown composition.

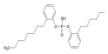
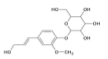
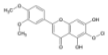
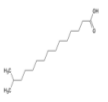
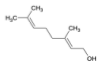
3.2. Qualitative screening of other organic contaminants in FCMs with SUPRAS-DIP-QTOF-MS/MS and library search.

The 18 positive samples were further analyzed with direct injection probe (DIP) coupled to high resolution mass spectrometry (QTOF). Data was acquired and treated as specified in section 2.4. Results of the tentatively identified compounds by library search are shown in Table 3.

A Level 2 of identification (probable structure) was applied according to Schymanski et al. 2014. In our study, this involved matching spectrum data from a library to obtain an unambiguous spectrum-structure match. In total, 14 compounds were identified with detection frequencies in the range of 5 and 33%. Five natural compounds with vegetal origin were attributed to the contained food in the package (they were present due to migration from food or insufficient clean-up before analysis), seven compounds were plastic additives (UV filters to prevent package degradation, fatty acids and phthalates) or synthesis intermediates and for the other two ones the use could not be identified.

Table 3. Identified compounds by DIP-QTOF-MS/MS and spectral library search

Formula	Error ppm	mSigma (isotopic pattern fit)	Main ion	Name	CAS	Application/use	Det. frequency	Structure
$C_8H_{12}N_2O$	9.5	198.2	$[M+H]^+$	2-Isopropyl-6-methyl-pyrimidin-4-ol	2814-20-2	Benzophenone derivatives synthesis intermediate, UV filter-type plastic additives	33%	
$C_9H_{11}NO_4$	9.2	170.3	$[M+H]^+$	3,4-Dihydroxy-L-phenylalanine	59-92-7	Synthesis intermediate, bio-additive which confers cohesion and adhesion to plastics, rubber bands and adhesives	5%	
$C_{12}H_{10}$	-2.9	20.6	$[M+H]^+$	Acenapthene	83-32-9	Synthesis intermediate of dyes and plastic production	5%	
$C_{19}H_{20}O_4$	3.6	5.5	$[M+H-H_2O]^+$, $[M+H]^+$	Benzyl-butyl-phthalate	85-68-7	Plasticizer-type plastic additive (confers durability, flexibility and other beneficial properties for materials)	10%	
$C_{20}H_{22}O_6$	4.2	13.4	$[M+H]^+$	Matairesinol	580-72-3	Plant lignan, high presence in oilseeds, whole grains, vegetables and fruits	10%	
$C_{17}H_{36}N_2O$	-6.1	9.3	$[M+H]^+$	N-[3-(Dimethylamino)propyl]dodecanamide	3179-80-4	Synthesis intermediate	33%	
$C_7H_{15}N_3O_4$	4.1	6.5	$[M-H]^-$	Tetrahydro-5-(2-hydroxyethyl)-1,3-bis(hydroxymethyl)-1,3,5-triazin-2(1H)-one	1852-21-7	Plastic additives, UV filter	8%	
$C_{13}H_{16}S$	-2.3	50.1	$[M-H]^-$	2-Pentyl-1-benzothiophene	89969-72-2	Unspecified	17%	

$C_{22}H_{44}O_2$	8.1	18.9	[M-H]-	Beheninic Acid	112-85-6	Fatty acid, as plastic additives have emollient function, emulsifier or lubricant or release agent, among other	8%	
$C_{28}H_{43}O_4P$	5.6	10.6	[M-H]-	Bis(2-octylphenyl) hydrogen phosphate	28258-94-8	Unspecified	25%	
$C_{16}H_{22}O_8$	-2.4	8.8	[M-H]-	Coniferin	531-29-3	Glycoside, plant metabolite	8%	
$C_{18}H_{16}O_7$	7.9	48.9	[M-H]-	Eupatilin	22368-21-4	Plant flavone (source from food)	8%	
$C_{16}H_{32}O_2$	0.4	13.8	[M-H]-	Isopalmitic Acid	32844-67-0	Fatty acid, as plastic additives have emollient function, emulsifier or lubricant or release agent, among other	8%	
$C_{10}H_{18}O$	9.6	12.1	[M-H]-	Nerol	106-25-2	Monoterpene, essential oils	33%	

4. Conclusions.

In this study, we evaluate the potential of using SUPRASs and ambient mass spectrometry for quantification and wide screening of organic contaminants in FCMs. The sample preparation consisted in rapid extraction step with SUPRAS of 1-decanol in ethanol:water mixtures (10:90, v/v) (1 min shaking with vortex, 0.4 mL SUPRAS per sample) and it was followed by analysis with ambient mass spectrometry. SUPRAS-ASAP-QqQ-MS/MS allowed the sensitive (LODs: 0.02-0.4 $\mu g \cdot g^{-1}$) and reproducible (≤20%) quantification of bisphenols A and derivatives and organophosphate flame retardants with aryl substituents in FCMs, two families of emerging contaminants which were selected to carry out this study. SUPRAS-DIP-QTOF-MS/MS and spectral library search was evaluated to carry out a suspect screening to identify other types of additives in the samples and to investigate the potential of the technique to multi-residue analysis. Results showed that food contact materials are complex and that around the half of the analyzed samples contained

bisphenols (n.d.-292 $\mu g \cdot g^{-1}$) or aryl-OPFRs (n.d.-14.2 $\mu g \cdot g^{-1}$) as well as other additives and unknown compounds, being FCMs a relevant human exposure route to contaminants.

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5.

Conclusiones

En esta sección se recogen las conclusiones obtenidas como resultado de las investigaciones realizadas en la presente Tesis Doctoral. Por un lado, se muestran las conclusiones generales de cada uno de los bloques en los que se encuentra dividida esta Tesis, y por otro, las conclusiones específicas derivadas de cada uno de los capítulos.

La primera parte de la Tesis (Bloque I), ha consistido principalmente en el desarrollo de tratamientos de muestra genéricos, rápidos, económicos, fáciles de implementar y respetuosos con el medio ambiente, con el fin de extraer, para posteriormente determinar y cuantificar, grupos de compuestos en muestras complejas. Dichos compuestos son contaminantes emergentes, para los cuales no existen restricciones legislativas (o es escasa o heterogénea) ni amplia información, pero para los que su estudio es de gran relevancia debido a su toxicidad y a su capacidad de migración y, por lo tanto, su capacidad para causar efectos adversos a corto y largo plazo en el ser humano y en el medio ambiente.

Para este fin, se han utilizado disolventes supramoleculares (SUPRASs), cuyas propiedades intrínsecas los convierten en excelentes extractantes de diversas familias de compuestos de matrices complejas. Además, cumplen también con muchos de los principios de la Química Sostenible.

Las investigaciones desarrolladas han supuesto un avance significativo en cuanto a la identificación de nuevos contaminantes (no detectados o poco investigados hasta la fecha) en muestras de polvo doméstico, alimentos y envases. En cuanto al polvo de edificios, el estudio de distintos microambientes, junto con la estimación de la exposición humana a través de la ingestión, permitió conocer el nivel de riesgo al que se encuentran expuestas las personas que trabajan o permanecen mucho tiempo en los lugares objeto de estudio, estando los resultados obtenidos siempre por debajo de los límites máximos de exposición establecidos. Por otro lado, el estudio de compuestos tóxicos en envases de alimentos y en comida cocinada, han permitido ampliar el conocimiento sobre la presencia de contaminantes emergentes en estas otras matrices complejas.

Las investigaciones llevadas a cabo en la segunda parte de la Tesis (Bloque II), consistieron en el uso por primera vez de SUPRASs y espectrometría de masas ambiental (AMS, de sus siglas en inglés *Ambient Mass Spectroemtry*), para llevar a cabo un tratamiento y análisis ultra-rápido de muestras de papel térmico y de envases de alimentos.

Capítulo I: Microextracción de bisfenol A y sustituyentes emergentes (desarrolladores del color en papel térmico) de muestras de polvo doméstico de lugares públicos basado en disolventes supramoleculares.

1. La matriz de polvo interior es compleja y heterogénea, ya que contiene desde fibras textiles y de papel, hasta cabello humano o animal, células y componentes minerales, entre otros. Gracias a sus propiedades de acceso restringido y de exclusión química, los

SUPRASs demostraron proporcionar un tratamiento de muestra adecuado para este tipo de matrices.

2. Los SUPRASs de anfifilos de cadena hidrocarbonada más corta (C_6), dan lugar a fases menos empaquetadas, con mayor superficie de contacto y con un mayor contenido en agua. Esto, junto a la formación de puentes de hidrógeno más energéticos, permitieron la extracción más eficiente de compuestos polares y medianamente polares (los bisfenoles en este caso).

3. El porcentaje de disolvente orgánico (tetrahidrofurano o THF) empleado en la preparación del SUPRAS, no afectó significativamente a la extracción, pero sí que incrementó el volumen de SUPRAS formado, obteniéndose menores factores de preconcentración. Por lo tanto, se seleccionó un porcentaje intermedio (16.7 % v/v).

4. Con respecto al porcentaje de anfifilo óptimo para la síntesis del SUPRAS, hay que tener en cuenta que una mayor cantidad de este también conlleva la generación de un volumen mayor de SUPRAS, disminuyéndose así el factor de preconcentración, Finalmente, y como solución de compromiso, se seleccionó un volumen de 200 µL.

5. El método de extracción desarrollado permitió el análisis de las muestras de polvo de una forma rápida (25 min), cuantitativa (recuperaciones en el rango 77 – 93%) y ecoeficiente. Los límites de detección (MDL) y cuantificación (MQL) del método fueron satisfactorios (0,5 – 10 y 1 – 20 ng·g^{-1}, respectivamente), y el efecto matriz fue aceptable (70 – 120%).

6. Se detectaron y cuantificaron los sustituyentes emergentes del BPA (BPS-MAE, D8 y TGSA, con concentraciones medias de 20, 23 y 22 ng·g^{-1}, respectivamente) por primera vez en muestras de polvo de tiendas de la provincia de Córdoba, donde el uso de papel térmico es muy frecuente. Se demostró así la capacidad de

migración de dichos compuestos al medio. BPS y BPF, empleados en mayor proporción en el mercado, estuvieron presentes a concentraciones mayores, con valores medios de 290 y 79 ng·g^{-1}, respectivamente.

7. Se concluyó que el polvo supone una ruta de exposición a estos compuestos adicional a la dérmica (mediante contacto con papel térmico), siendo necesaria la evaluación del riesgo para la salud de las personas que trabajan/permanecen diariamente en lugares donde el uso de tickets es elevado (tiendas, restaurantes, etc.).

Capítulo II: Análisis de bisfenol A y sustituyentes emergentes en polvo doméstico del sur de España.

1. El método desarrollado en el capítulo anterior fue aplicado a 47 muestras de viviendas (habitaciones y salones), coches, oficinas y tiendas, lo cual permitió llevar a cabo un estudio más exhaustivo de la presencia de BPA y sus sustitutos en otros ambientes de interior y una estimación de la exposición humana por ingestión.

2. Los resultados mostraron que BPA, BPS y BPF fueron los compuestos más detectados y en mayor concentración (<LOD – 13.846, <LOD – 736 y <LOD – 659 ng·g^{-1}, respectivamente) debido al uso tan amplio del BPA y a que el BPS y el BPF son los sustituyentes más comúnmente utilizados.

3. Las concentraciones del resto de sustituyentes (BPS-MAE, D8 y TGSA) fueron más bajas (<LOD – 529, <LOD – 128 y <LOD – 356 ng·g^{-1}, respectivamente), pero con porcentajes de detección relativamente altos (50 – 90%) en lugares públicos, donde se explica por el elevado uso de los tickets y/o por la presencia de fuentes de contaminación no identificadas. Las frecuencias de detección fueron también altas (55 – 82%) en interiores de coches,

lo cual sugiere la posibilidad de que sean utilizados en la fabricación de materiales usados en el interior de los mismos.

4. Se encontraron correlaciones positivas y estadísticamente significativas entre varios compuestos, como por ejemplo entre TGSA y D8 cuando se compararon todas las muestras. BPA mostró también correlaciones positivas con estos dos sustituyentes en las muestras de los lugares públicos. La presencia simultánea de estos pares de contaminantes no ha sido citada en estudios previos y sugiere que puedan proceder de mezclas empleadas en la fabricación de materiales no identificados.

5. También se encontraron correlaciones positivas y estadísticamente significativas entre BPF y D8 en muestras de lugares públicos. Sin embargo, BPF no se usa en papel térmico, por lo que su uso en otros materiales explicaría esta correlación.

6. BPA y BPS estuvieron también correlacionados positivamente, lo cual se explica porque son los bisfenoles más comúnmente usados.

7. Los valores medios de la estimación de la exposición humana a los sustituyentes emergentes del BPA mediante ingestión de polvo fueron de <0,1, <0,1 y 0,4 ng/día en adultos y de <0,1, 0,1 y 1,1 ng/día en niños, para BPS-MAE, D8 y TGSA, respectivamente. Estos valores estuvieron en concordancia con su limitado uso en el mercado en comparación con el BPA, BPS y BPF (valores medios de exposición de 42,9, 3,9 y 1,4 ng/día en adultos y 86,6, 7,3 y 2,9 ng/día en niños, respectivamente).

8. Aunque la exposición calculada de los compuestos emergentes BPS-MAE, D8 y TGSA fue baja, se espera que en el futuro el uso de los sustituyentes aumente debido a las restricciones del BPA en papel térmico desde el año 2020.

Capítulo III: Microextracción de retardantes de llama aril-fosforados de polvo doméstico de casas y centros de educación en España basada en disolventes supramoleculares.

1. La metodología desarrollada en el Capítulo I también se aplicó a otro grupo de compuestos emergentes, los retardantes de llama aril-organofosforados (aryl-OPFRs), en muestras de polvo. En concreto fueron 16 muestras de centros educativos (5 de guarderías, 3 de escuelas primarias, 2 de institutos y 6 aulas universitarias ubicadas en el Campus de Rabanales) y 22 de viviendas (salones y dormitorios).

2. El método de extracción tuvo una precisión aceptable (expresada como desviación estándar relativa o RSD, 0,6 – 19%), con límites de detección (MDL) y cuantificación (MQL) del método en los intervalos de 0,2 – 5 ng·g^{-1} y 0,5 – 10 ng·g^{-1}, respectivamente.

3. Por primera vez se detectaron y cuantificaron algunos aryl-OPFRs poco estudiados, (IDPP, BDP y RDP), con concentraciones medias de 573, 16 y 52 ng·g^{-1}, respectivamente, en muestras de polvo doméstico de centros educativos, junto con otros más conocidos como TPHP, EHDPP y CDP, que estuvieron presentes a concentraciones medias de 2.081, 5.377 y 62 ng·g^{-1}, respectivamente.

4. TPHP fue el compuesto con mayor abundancia relativa en casas (calculada dividiendo la mediana del compuesto entre la suma de las medianas de todos los compuestos), con un valor del 69%, lo cual se explica por ser el aryl-OPFR más producido y utilizado. Por otro lado, EHDPP e IDPP fueron los compuestos con mayor abundancia relativa en centros educativos, ambos con valores del 33%.

5. En general, los compuestos fueron detectados en concentraciones más altas en centros educativos que en casas, especialmente en

clases de universidad (posiblemente debido a su mayor tamaño, menor ventilación, diferentes materiales de construcción, etc.).

6. La mitad de las correlaciones positivas entre estos compuestos fueron estadísticamente significativas, lo que podría indicar que provienen de la misma fuente de origen.

7. La exposición por ingestión de polvo a los aryl-OPFRs fue igual para los niños que iban a guarderías (con valores medios de 0,04 – 1,71 ng·Kg de peso^{-1} · día^{-1}) que para los que permanecían en casa (con valores medios de 0,01 – 2,02 ng·Kg de peso^{-1} · día^{-1}). Sin embargo, sí que hubo mucha diferencia entre los niños que van a la guardería y los adultos que trabajan allí (con valores medios de 0 – 0,11 ng·Kg de peso^{-1} · día^{-1}), debido a que los niños pasan más tiempo en el suelo y el contacto mano-boca es más frecuente.

8. El nivel de exposición de los adultos que trabajan o estudian en universidades (con valores medios de 0 – 0,37 ng·Kg de peso^{-1} · día^{-1}) es mayor que los que están en otros centros educativos.

9. Todos los niveles de exposición calculados estuvieron por debajo de las dosis de referencia recomendadas.

Capítulo IV: Caracterización de un nuevo disolvente supramolecular sostenible y aplicación en la determinación de oxy-PAHs en muestras de carne, marisco y pescado.

1. La síntesis y caracterización de un nuevo SUPRAS basado en el uso de mezclas de un disolvente verde (2-metil-tetrahidrofurano, 2-MeTHF), agua y 1-hexanol permitió el desarrollo de un método de extracción más sostenible.

2. El volumen de SUPRAS formado fue linealmente proporcional al porcentaje de 2-MeTHF, siendo esta relación normalmente

exponencial (como ocurre con el THF) en la formación de los SUPRASs. Esto se debe posiblemente al rango tan limitado de formación del nuevo SUPRAS (2.5 – 12.5% v/v) en comparación con el de THF (80 – 90% v/v).

3. La estructura del SUPRAS se estudió por microscopía, observándose estructuras hexagonales inversas, al igual que ocurre con los SUPRASs de alcoholes en THF.

4. Las cadenas hidrocarbonadas más cortas en la molécula anfifílica incrementaron la cantidad de agua y de disolvente orgánico en los SUPRASs. Este mayor contenido en agua, junto con la formación de puentes de hidrógeno más energéticos, permitió la extracción más eficiente de compuestos medianamente polares (los oxy-PAHs en este caso) con los SUPRASs de 1-hexanol con respecto a los SUPRASs de 1-octanol o 1-decanol.

5. El SUPRAS se formó en una etapa previa y se añadió a la muestra, junto con la disolución de equilibrio. Se seleccionaron como óptimos para la formación del SUPRAS porcentajes de 2-MeTHF de 5% v/v para matrices de carne y 7.5% v/v para matrices de pescado, empleando porcentajes de anfifilo del 5% v/v, ya que proporcionaron mejores recuperaciones y menor efecto matriz.

10. Las precisiones intra- e inter-día del método fueron aceptables (expresadas como desviación estándar relativa o RSD, 0,06 – 18,5% y 6,9 – 17,4%, respectivamente). Los límites de detección (MDL) y cuantificación (MQL) del método estuvieron en intervalos de 0,2 – 1,3 ng $\cdot g^{-1}$ y 0,4 – 4 ng $\cdot g^{-1}$, respectivamente.

11. Los oxy-PAHs fueron encontrados en 7 muestras de un total de 19, en concentraciones de 3,5 a 12,6 ng $\cdot g^{-1}$ (expresadas como sumatorio de todos los oxy-PAHs en estudio).

Capítulo V: Determinación de diferentes grupos de PFAS en materiales de envasado de alimentos de diferentes restaurantes de comida rápida en Francia.

1. Se puso a punto un método de extracción con un disolvente orgánico (metanol), seguido de extracción en fase sólida (SPE, de sus siglas en inglés solid phase extraction), previo a análisis con cromatografía líquida y espectrometría de masas en tándem para el análisis de varios grupos de PFAS: ácidos perfluorocarboxílicos (PFCAs), ácidos perfluorosulfónicos (PFSAs), sulfonamidas y fluorotelómeros de ésteres de fosfato (PAPs).

2. Tres de los compuestos, en concreto el ácido perfluorohexanoico, (PFHxA), el 6:2 fluorotelómero de ácido sulfonico (6:2 FTS) y el 6:2/6:2 fluorotelómero de diésteres de fosfato (6:2/6:2 diPAP), fueron encontrados en todas las muestras (con concentraciones medias de 0,3, 0,03 y 0,1 ng·g^{-1}, respectivamente).

3. Los PFCAs de cadena corta fueron encontrados en mayor concentración, con medias de 0,3, 0,09 y 0,3 ng·g^{-1} para el ácido perfluorobutanoico (PFBA), el ácido perfluoropentanoico (PFPeA) y PFHxA, respectivamente, pero con menor frecuencia que los de cadena media (C_7-C_{10}) y larga (C_{11}-C_{18}). Esto puede ser debido a las restricciones legislativas en el uso de PFCAs de cadena media y larga (promoviendo el reemplazo por los de cadena corta), y al hecho de que los PFCAs de cadena corta deben añadirse en mayor cantidad para cumplir la misma función que hacen los de cadena media y larga.

4. Algunos de los PFSAs se encontraron en concentraciones similares a los PFCAs (0,03 – 0,2 ng·g^{-1}) y con similar frecuencia.

5. El grupo predominante en las muestras fue el de los PAPs, resultado que era de esperar, ya que son compuestos utilizados en

los envases de alimentos en mayor proporción con respecto al resto de PFAS.

6. Se observaron algunas correlaciones positivas y estadísticamente significativas entre compuestos, sugiriendo rutas de degradación o fuentes de origen similares. Algunas de ellas son, por ejemplo, entre el ácido perfluorononanoico (PFNA) y el ácido perfluorooctanoico (PFOA), debido a que ambos compuestos son productos de biodegradación del mismo precursor, o entre PFOA y los PAPs 6:2/6:2 diPAP y 8:2/8:2 diPAP, lo cual se explica debido a que estos dos últimos se degradan en el primero.

Capítulo VI: Microextracción basada en disolventes supramoleculares para la detección rápida de bisfenoles mediante el uso de sonda y espectrometría de masas ambiental.

1. Se desarrolló un método rápido y simple basado en el uso de SUPRASs contenidos en capilares de vidrio (sonda) para la extracción de bisfenoles, previo al análisis mediante espectrometría de masas ambiental (*Ambient Mass Spectrometry*, AMS).

2. El volumen de SUPRAS contenido en la sonda era de 1 a 2 μL. La sonda con SUPRAS se ponía en contacto directo con la muestra (papel térmico) durante 10 segundos y el extracto se analizaba después mediante AMS durante 1 minuto.

3. Los SUPRASs óptimos fueron aquellos formados por agregados inversos de alcoholes de cadena media, disolvente orgánico y agua, ya que su ionización en la fuente es muy baja.

4. El uso de ácidos carboxílicos como anfifilo no dio buenos resultados debido al fuerte efecto de supresión de la ionización en la fuente en modo negativo.

5. Los alcoholes simples proporcionaron mejores resultados que los dioles, debido a que estos últimos daban lugar a SUPRASs con más contenido en agua partiendo de las mismas condiciones iniciales de síntesis, por lo que el único bisfenol que se extrajo mejor con los dioles fue el más polar (BPS, con logP = 1.2). El resto, al ser medianamente polares, se extrajeron mejor con el alcohol simple.

6. La cadena más corta de alcohol simple ensayada para la formación del SUPRAS (C_6) proporcionó mayor eficacia de extracción. Sin embargo, a medida que aumentaba la longitud de la cadena del anfifilo, disminuía la desviación estándar relativa (o RSD) de las medidas (4 – 25% para C_6, 2 – 16% para C_{10} y 3 – 14% para C_{14}), por lo que se seleccionó una longitud de cadena intermedia (C_{10}) como solución de compromiso.

7. No hubo diferencias en la extracción utilizando SUPRASs sintetizados con etanol y con THF, por lo que se seleccionó el primero como óptimo al ser menos tóxico. La cantidad de este en la disolución de síntesis inicial tampoco varió las recuperaciones de los bisfenoles significativamente, por lo que se seleccionó el porcentaje más bajo ya que proporcionaba SUPRASs más viscosos y menos volátiles, lo cual favoreció su introducción y permanencia en el capilar de vidrio durante la extracción, además del ahorro en reactivos y generación de residuos.

8. Se aplicó la metodología a 62 muestras de papel térmico (23 procedentes de tiendas de alimentación y restaurantes, 7 de cajeros automáticos, 10 de gasolineras y transporte público y 22 de otras tiendas, tales como de ropa, cosmética, papelería, etc.).

9. BPA y BPS fueron los bisfenoles más abundantes en las muestras de papel térmico (con frecuencias de detección de 44% y 53%, respectivamente). Estos resultados sugieren que el BPA está siendo reemplazado por el BPS debido a las restricciones sobre su uso en papel térmico.

10. Otros sustituyentes del BPA, como el Pergafast 201, TGSA o D8, no son comúnmente usados todavía y se encontraron en menor abundancia (con frecuencias de detección de 1,6% para los dos primeros y 0% para el D8).

Capítulo VII: Determinación de contaminantes orgánicos en envases de alimentos mediante la extracción con disolventes supramoleculares y análisis con espectrometría de masas ambiental.

1. En base a los resultados obtenidos en el capítulo anterior, se aplicó un tratamiento genérico con SUPRASs de agregados inversos de 1-decanol en mezclas de etanol y agua y un posterior análisis con espectrometría de masas ambiental (*Ambient Mass Spectrometry*, AMS) de baja resolución (triple cuadrupolo) y de alta resolución (QTOF) para el análisis de envases de alimentos.

2. Se seleccionó un conjunto de bisfenoles y retardantes de llama aril-organofosforados (aryl-OPFRs) como compuestos diana para la cuantificación, debido a su presencia en envases de alimentos plásticos, que son uno de los materiales más comunes para este fin.

3. Los LODs (0,3 – 17 $\mu g \cdot L^{-1}$ para los bisfenoles y 0,7 – 3 $\mu g \cdot L^{-1}$ para los aryl-OPFRs) y LOQs (1 – 50 $\mu g \cdot L^{-1}$ para los bisfenoles y 2 – 10 $\mu g \cdot L^{-1}$ para los aryl-OPFrs) obtenidos con AMS para cada compuesto fueron un orden de magnitud mayor que los LODs y LOQs obtenidos con cromatografía líquida en otros estudios (Capítulos I, II y III), lo que se explicaría por los bajos volúmenes de inyección con la sonda (apenas 1 ó 2 µL) y los valores de señal/ruido más bajos en esta técnica al no haber separación cromatográfica. Sin embargo, fueron lo suficientemente bajos para el análisis cuantitativo de trazas en materiales.

4. Los bisfenoles fueron encontrados en mayores concentraciones y con más frecuencia (~30%, excepto TGSA, que solo se encontró en

una muestra) que los aryl-OPFRs, de los cuales solo se encontraron dos de los seis estudiados (EHDPP y CDP) en el 12.5-22.5% de las muestras.

5. Se identificaron además otros 14 compuestos mediante cribado no dirigido con QTOF de alta resolución y búsqueda en librería espectral, los cuales tuvieron frecuencias de detección entre el 5 y el 33%.

6. Cinco de ellos eran compuestos de origen vegetal, que posiblemente habrían migrado de la comida que contenía el envase. Otros 7 compuestos fueron aditivos plásticos (añadidos para proteger al envase de la degradación, como filtros ultravioleta o ftalatos) o compuestos intermedios de síntesis, y otros dos no pudieron ser identificados.

7. Los resultados revelaron que los materiales en contacto con los alimentos tienen una composición compleja, siendo una ruta importante de exposición humana a contaminantes.

5.

Conclusions

Conclusions derived from the research developed in this Doctoral Thesis are presented in this section.

At first, general conclusions from each block in which this Thesis is divided, are presented. After that, specific conclusions of each chapter are introduced.

The first part (Block I) deals with the development of faster, more economic and environmental-friendly generic sample treatments with easy implementation for the determination of emerging contaminants. These pollutants are those with limited or nonexistent legislative restrictions, and for which information about their presence and distribution in the environment is still scarce. The study of emerging contaminants is of great relevance due to their potential toxicity and migration capacity, and therefore their capacity to produce adverse effects of short and long term to human health and the environment.

Supramolecular solvents (SUPRASs) were used as extractants, due to their intrinsic properties which make them excellent candidates for the extraction of a wide variety of compounds in complex matrices. In addition, they meet some of the Green Chemistry principles.

The developed research has made advances in terms of identification of non-detected or under-researched contaminants in indoor dust samples, food and food packaging materials. Regards to the indoor dust, both the study of different microenvironments and the estimation of human exposure by ingestion provided knowledge about the contamination levels to which workers in these indoor places are exposed to. These levels were always under the maximum established exposure limits. On the other hand, the study of toxic compounds in food packages and cooked food provided further knowledge about the presence of emerging contaminants in these complex matrices.

In the second part (Block II), SUPRASs were combined with Ambient Mass Spectrometry (AMS) for the first time to treat and analyze samples of thermal paper and food packages quickly.

Chapter I: Supramolecular solvent-based microextraction of emerging bisphenol A replacements (colour developers) in indoor dust from public Environments.

1. The indoor dust matrix is complex and heterogenous, it contains from textile and paper fibers to human or animal hair, cells and mineral compounds, among others. Because of their chemical exclusion and restricted access properties, SUPRASs provided a suitable sample treatment for this type of matrices.

2. SUPRASs made up of amphiphiles with the shortest hydrocarbon chain (C_6) provide less packaged phases, with higher contact surface and higher water content. This fact, together with more

energetic hydrogen bonds enhanced the extraction of polar and medium polar compounds (bisphenols in this case).

3. The percentage of organic solvent (tetrahydrofuran, THF) in SUPRASs formation did not significantly affect the extraction efficiency. However, the volume of generated SUPRAS increased, giving rise to lower preconcentration factors. For that reason, an intermediate percentage of THF was selected (16.7%).

4. With regards to the percentage of amphiphile for SUPRAS formation, the higher the value, the higher the SUPRAS volume and, consequently, the lower the preconcentration factors. For that reason, a volume of 200 μL of amphiphile was selected as compromise solution.

5. The developed extraction method permitted a fast (25 min), quantitative (recoveries ranged between 77 – 93%) and environmental-friendly analysis of indoor dust samples. Method detection (MDL) and quantification limits (MQL) were satisfactory (0.5 – 10 and 1 – 20 $ng \cdot g^{-1}$, respectively) and matrix effect were acceptable (70 – 120%).

6. Emerging substitutes of BPA (BPS-MAE, D8 and TGSA) were detected and quantified (with mean concentrations of 20, 23 and 22 $ng \cdot g^{-1}$, respectively) for the first time in indoor dust samples of shops from Córdoba, where thermal paper use is very frequent. Migration capacity of these compounds could be demonstrated in this way. BPS and BPF, which are more commonly used, were present at higher concentrations, with mean values of 290 and 79 $ng \cdot g^{-1}$, respectively.

7. The ingestion of indoor dust can be considered an additional exposition route to dermal contact with thermal paper for bisphenols. People who work or stay daily in places where the use of tickets is high (shops, restaurants, etc.) may be at risk.

Chapter II: Emerging bisphenol A replacements (colour developers) in indoor dust from Spain.

1. The method described in the previous chapter was applied to 47 samples of living rooms and bedrooms, cars, offices and shops. This permitted to perform a more exhaustive study of the presence of BPA and its substitutes in other indoor environments and to estimate the human exposure by ingestion.

2. Results showed that BPA, BPS and BPF were the compounds more detected and at higher concentrations (<LOD – 13,846, <LOD – 736 and <LOD – 659 ng $\cdot g^{-1}$, respectively). The wide use of BPA and the fact that BPS and BPF are the most common substitutes explain these findings.

3. Concentration of the rest of analytes (BPS-MAE, D8 and TGSA) were lower (<LOD – 529, <LOD – 128 y <LOD – 356 ng $\cdot g^{-1}$, respectively), but with high detection percentages (50 – 90 %) in public establishments (which can be explained by the high use of tickets in these places or by the presence of non-identified contamination sources). Detection frequencies were also high (55 – 82%) in cars, which suggest the possibility of their use in the fabrication of materials related with car interiors.

4. Statistically significant positive correlations were found between several compounds, such as between TGSA and D8, when all samples were compared. BPA also showed positive correlations with both analytes in samples of public establishments. The simultaneous presence of these pairs of contaminants has not been cited in previous studies, suggesting that they could come from mixtures employed in the fabrication of non-identified materials.

5. Statistically significant positive correlations were also found between BPF and D8 in samples of public establishments.

However, BPF is not used in thermal paper, so its use in other materials could explain this correlation.

6. BPA and BPS were also positively correlated, which can be explained by the fact that they are the most commonly used bisphenols.

7. Human exposure by dust ingestion (mean values) was <0.1, <0.1 and 0.4 ng/day in adults and <0.1, 0.1 and 1.1 ng/day in toddlers, for BPS-MAE, D8 and TGSA, respectively. These values were in accordance with their limited use in the industry in comparison with BPA, BPS and BPF (mean values of 42.9, 3.9 and 1.4 ng/day in adults and 86.6, 7.3 and 2.9 ng/day in toddlers, respectively).

8. Although the estimated exposure by dust ingestion to BPS-MAE, D8 and TGSA was low, it is expected that their use increases in the future due to the restrictions of the use of BPA in thermal paper since 2020.

Chapter III: Supramolecular solvent-based microextraction of aryl-phosphate flame retardants in indoor dust from houses and education buildings in Spain.

1. The methodology reported in Chapter I was also applied to a group of emerging compounds, namely aryl-organophosphate flame retardants (aryl-OPFRs). Samples were indoor dust, specifically 16 samples from educative buildings (5 kindergartens, 3 primary schools, 2 high schools and 6 University classrooms) and 22 samples from houses (living rooms and bedrooms).

2. The extraction method had an acceptable precision (expressed as relative standard deviation or RSD, 0.6 – 19%), with method detection (MDL) and quantification limits (MQL) between 0.2 – 5 $ng \cdot g^{-1}$ and 0.5 – 10 $ng \cdot g^{-1}$, respectively.

3. For the first time, some under-researched aryl-OPFRs (IDPP, BDP and RDP) were detected and quantified with mean concentrations of 573, 16 and 52 ng·g^{-1}, respectively, in indoor dust samples from education buildings, together with other well-known aryl-OPFRs, namely TPHP, EHDPP and CDP, which were present with mean concentrations of 2,081, 5,377 and 62 ng·g^{-1}, respectively.

4. TPHP was the compound with the highest relative abundance in houses (69%, which was calculated by the division between the median of TPHP and the sum of all compounds medians). This can be explained due to the fact that TPHP is the most produced and used aryl-OPFRs. EHDPP and IDPP were the compounds with higher relative abundance in educative buildings, both with values of 33%.

5. In general, compounds were detected at higher concentrations in educative buildings than in houses, especially at University classrooms (possibly due to their higher size, less ventilation, different building materials, etc.).

6. The half of the positive correlations between these compounds were statistically significant, which can be explained with the fact that they may have similar origin sources.

7. Exposure to aryl-OPFRs by dust ingestion was similar for toddlers that go to kindergartens (with mean values of 0.04 – 1.71 ng·Kg body $weight^{-1} \cdot day^{-1}$) than those who stay at home (with mean values of 0.01 –2.02 ng·Kg body $weight^{-1} \cdot day^{-1}$). However, there were differences between toddlers that go to kindergartens and adults that work there (with mean values of 0 – 0.11 ng·Kg body $weight^{-1} \cdot day^{-1}$), due to the fact that toddlers spend long time playing on floors and that the hand-to-mouth contact is very frequent.

8. The exposition level in adults that work or study at the University (with mean values of 0 – 0,37 ng·Kg body weight^{-1} · day^{-1}) was higher than that of adults than work in other education buildings.

9. All exposure levels were under the recommended reference doses.

Chapter IV: Characterization of a new sustainable supramolecular solvent and application to the determination of oxy-PAHs in meat, seafood and fish tissues.

1. The synthesis and characterization of a new SUPRAS based on the use of mixtures of a green solvent (2-methyl-tetrahydrofuran, 2-MeTHF), water and 1-hexanol, allowed the development of a more sustainable extraction method.

2. SUPRAS volume was lineally dependent to the percentage of 2-MeTHF in the formation of SUPRASs, although this relation is usually exponential (such as with THF). This can be due to the limited THF range for the new SUPRAS formation (2.5 – 12.5% v/v) in comparison with that of SUPRASs formed with THF (80 – 90% v/v).

3. The SUPRAS was studied by electron microscopy, showing inverse hexagonal structures, as with SUPRASs made up of alcohols in THF.

4. Shorter hydrocarbon chain lengths of the amphiphilic molecule increased both the water and the organic solvent amount in SUPRAS. The higher water content, together with the formation of more energetic hydrogen bonds, allowed the more efficient extraction of medium polar compounds (oxy-PAHs in this case) with SUPRASs made of 1-hexanol regarding to those made of 1-octanol or 1-decanol.

5. The SUPRAS was formed in a previous step and it was added to the sample together with the equilibrium solution. Optimal percentages of 2-MeTHF, which gave better recoveries and lower matrix effects, were 5% v/v for meat and 7.5% v/v for fish, both with 5% v/v of amphiphile.

6. Intra- and inter-day precision was acceptable (expressed as relative standard deviation or RSD, 0.06 – 18.5% and 6.9 – 17.4%, respectively). Method detection (MDL) and quantification limits (MQL) were in the ranges of 0.2 – 1.3 ng·g^{-1} and 0.4 – 4 ng·g^{-1}, respectively.

7. Oxy-PAHs were found in 7 out of 19 samples, in concentrations that ranged 3.5 – 12.6 ng·g^{-1} (expressed as the sum of all the target compounds).

Chapter V: Analysis of several PFAS groups in food packaging material from fast-food restaurants in France.

1. An extraction method with an organic solvent (methanol) was developed, followed by solid phase extraction (SPE), prior to analysis with liquid chromatography coupled to mass spectrometry in tandem for the analysis of several groups of PFAS: perfluorocarboxylic acids (PFCAs), perfluorosulphonic acids (PFSAs), sulphonamides and fluorotelomer phosphate esters (PAPs).

2. Perfluorohexanoic acid (PFHxA), 6:2 fluorotelomer sulphonic acid (6:2 FTS) and 6:2/6:2 fluorotelomer phosphate diester (6:2/6:2 diPAP) were found in all samples (with mean concentrations of 0.3, 0.03 and 0.1 ng·g^{-1}, respectively).

3. Short chain PFCAs were found at higher concentrations, with mean values of 0.3, 0.09 and 0.3 ng·g^{-1} for perfluorobutanoic acid

(PFBA), perfluoropentanoic acid (PFPeA) and PFHxA, respectively, but with less frequency than the median (C_7-C_{10}) and long chain (C_{11}-C_{18}) acids. This can be due to the legislative restrictions in the use of median and long chain PFCAs (promoting the replacement by those of shorter chain length) and because of the fact that short chain PFCAs should be added in higher amounts to fulfill the same functions than those of medium and long chain length.

4. Some PFSAs were found at similar concentrations to PFCAs (0.03 – 0.2 ng·g^{-1}) and with similar frequencies.

5. PAPs were the predominant group. This was expected since they are the most commonly used PFAS in food packages.

6. Some statistically significant positive correlations were observed between compounds, which suggests similar degradation routes or origin sources. Some of them were, for example, between perfluorononanoic acid (PFNA) and perfluorooctanoic acid (PFOA), due to the fact that both compounds are biodegradation products from the same precursor. Other correlation was between PFOA and 6:2/6:2 diPAP and 8:2/8:2 diPAP, which can be explained due to the fact that PFOA is a degradation product from both PAPs.

Chapter VI: Supramolecular solvent-based microextraction probe for fast detection of bisphenols by ambient mass spectrometry.

1. A fast and simple method based on SUPRASs loaded in glass capillaries (probes) was developed. It was used for the extraction of bisphenols, prior to analysis with ambient mass spectrometry (AMS).

2. SUPRAS volume loaded in the probe was 1 or 2 μL. The probe with the SUPRAS was placed in direct contact with the sample (thermal

paper) during 10 seconds, and it was measured by AMS during 1 minute.

3. Optimal SUPRASs were those formed by inverse aggregates of medium chain alcohols, organic solvent and water, given that their ionization in the MS source is negligible.

4. The use of carboxylic acids as amphiphile did not give good results due to the strong suppression effects in the MS source in negative mode.

5. Simple alcohols gave better results than diols, because their SUPRASs contain a higher amount of water under the same synthesis conditions. This resulted in a good extraction efficiency for the most polar bisphenol (BPS, with logP= 1.2), but not for the rest, due to the fact that they are moderately polar, so they were better extracted with SUPRASs made up from the simple alcohol.

6. The simple alcohol with the shortest chain employed for SUPRAS formation (C_6) provided the highest extraction efficiency. However, as the amphiphile chain length increased, the relative standard deviation (RSD) of the measures decreased (4 – 25% for C_6, 2 – 16% for C_{10} and 3 – 14% for C_{14}), so that an intermediate chain length (C_{10}) was selected as an optimal compromise between sensibility and precision.

7. There were no differences in extraction between SUPRASs synthesized with ethanol or with tetrahydrofuran (THF), so the first one was selected as optimal due to its lower toxicity. There were neither significant differences in the recovery of bisphenols when the percentage of ethanol in the initial solution for SUPRAS synthesis was varied, so that the lowest percentage was selected. Low percentages of organic solvent in the synthesis solution resulted in SUPRASs that were more viscous and less volatile, which facilitated their introduction and permanence onto the glass

capillary during the extraction. Additionally, less reagents were used resulting in less waste generation.

8. The proposed method was applied to 62 thermal paper samples (23 coming from grocery shops and restaurants, 7 from ATMs, 10 from gas stations and public transports, and 22 from other shops, such as clothes, cosmetics, etc.)

9. BPA and BPS were the most abundant in thermal paper samples (with detection frequencies of 44% and 53%, respectively). These results suggest that BPA is being replaced by BPS due to the restrictions on its use in thermal paper.

10. Other BPA substitutes such as Pergafast 201, TGSA or D8 were scarcely found (with detection frequencies of 1.6% for the first ones and 0% for the las one), so this suggest that they are not still commonly used.

Chapter VII: Supramolecular solvent extraction and ambient mass spectrometry for the determination of organic contaminants in food packaging material.

1. Based on the results reported in the previous Chapter, a generic treatment with SUPRASs formed by inverse aggregates of 1-decanol with ethanol and water mixtures was applied to 40 food packaging materials, prior to analysis by low-resolution (triple quadrupole) ambient mass spectrometry (AMS) and high-resolution (QTOF) AMS.

2. Bisphenols and aryl-organophosphate flame retardants (aryl-OPFRs) were the target compounds for quantification, due to their presence in plastic food packaging materials.

3. Instrumental LODs (0.3 – 17 μg·L^{-1} for bisphenols and 0.7 – 3 μg·L^{-1} for aryl-OPFRs) and LOQs (1 – 50 μg·L^{-1} for bisphenols and 2 – 10 μg·L^{-1} for aryl-OPFRs) obtained with AMs for each compound were one order of magnitude higher than those obtained by liquid chromatography in the other studies (Chapters I, II and III). This could be explained by the low injection volumes with the probe (1 or 2 μL) and the lower signal to noise ratio values of this technique which does not use chromatographic separation. However, they were low enough for trace analysis in materials.

4. Bisphenols were found in higher concentrations and with more frequency (~30%, except TGSA, which was only found in one out of forty samples) than aryl-OPFRs. Aryl-OPFRs (EHDPP and CDP) were present in 12.5-22.5% of the samples.

5. In addition, 14 compounds were identified through broad-spectrum screening with QTOF and searching on an open access spectral library. They had detection frequencies between 5 and 33%.

6. Five of them were of plant origin, maybe attributed to the contained food in packages. Other 7 compounds were plastics additives (added to protect the package from degradation, such as UV filters or phthalates) or synthesis intermediates, and other two compounds could not be identified.

7. Results showed that food contact materials have a complex composition, being an important exposure route for humans to contaminants.

6.

Otras publicaciones científicas

La doctoranda es coautora de una patente, relacionada con la temática de la Tesis, y por otro lado, también es coautora de 1 artículo científico y 1 capítulo de libro, publicados antes de comenzar la Tesis.

1. Dueñas-Mas, M.J., Ballesteros-Gómez, A., Rubio, S. **Referencia:** ES2932558 A1. **Título:** Procedimiento para la obtención de licopeno a partir de subproductos del tomate basado en el uso de biodisolventes supramoleculares. **País de prioridad:** España. **Fecha publicación:** 20.01.2023. **Solicitante:** Universidad of Córdoba.
2. Dueñas-Mas, M.J., Soriano, M. L., Ruiz-Palomero, C., Valcárcel, M. 2018. Modified nanocellulose as promising material for the extraction of gold nanoparticles. Microchem. J. 138, 379-383.
3. Soriano, M. L., Dueñas-Mas, M.J. 2018. Promising Sensing Platforms Based on Nanocellulose. Carbon-Based Nanosensor Technology. Springer Series on Chemical Sensors and Biosensors (ISBN 978-3-030-11864-8) 17, 273-301.

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(57) Resumen:
La presente invención se refiere a un procedimiento para la obtención y enriquecimiento de licopeno a partir de residuos procedentes del procesamiento de tomates, basado en el uso de biodisolventes supramoleculares o bioSUPRAS, y al uso del licopeno así obtenido como aditivo alimentario.

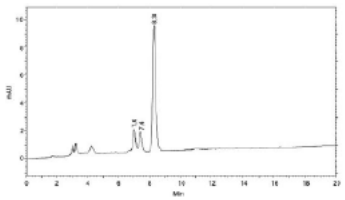

FIG.1

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Modified nanocellulose as promising material for the extraction of gold nanoparticles

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ABSTRACT

Increasing number of engineering nanoparticles (NPs) in consumer products is unstoppable even after the toxic effect of metallic-based nanomaterials stated more than a decade ago; thus, selective methods for detecting metallic NPs are highly demanded and of great importance. A simple and rapid approach for detecting gold NPs (AuNPs) using ecofriendly sulfonated nanocellulose (*s*-NC) as sorbent material is described. The interaction between *s*-NC and AuNP is based on the affinity of sulfur atoms towards metals. We found that the use of cationic surfactant substantially benefitted the extraction and preconcentration of AuNPs by virtue of the NP stabilization. Good linear correlations were found in a concentration range spanned from 7 to 20 μg/mL with a detection limit of 0.26 μg/mL. Furthermore, the proposed method was successfully applied to detect AuNPs in presence of other nanowastes, opening new opportunities of creating functional materials to collect and store nanoobjects for further uses. Further experiments are directed for reaching a generalized method towards the analysis of a bigger variety of NPs covering the trending topic third facet of the analytical nanoscience and nanotechnology.

1. Introduction

In recent years, the fascinating physicochemical properties of nanomaterials had entailed an exponential growth of applications, which includes many areas such as medicine, electronics, catalysts, cosmetics, food, and textile. With the nanotechnology promise to benefit the Society, this progress has forced the market with a vast of consumer goods containing large quantities of nanomaterials. As all revolutionary technologies, the impact of this growth on human health and environment is undeniable and a myriad of problems and consequences is coming to be faced. Nanotoxicology [1] is still in its infancy and there exist controversy around nanoparticle (NP) safety, which is stated to be dependent not only on their particle shape and size distribution but also on their chemical composition and stability, i.e., which is governed by their surface (both functionalities and charges) [2].

In this respect, pollution caused by nanotechnology has become one of the most urgent concerns for protecting the ecosystem [3]. Of great interest is the case of metallic NPs [4,5] by virtue of their antimicrobial properties, being able to interact with biomolecules, cells and even organs of living organisms for its nanosize and large surface area. On the other hand, it is expected that NPs accumulate in environment, for instance after their recent applicability as promising pesticides [6], or by their released from wasted consumer products. In reaction to this, the analytical community has paid attention in creating low-cost sophisticated analytical methods with ecofriendly sorbent materials for the detection, quantification and storage of hazardous NPs.

Most of methods described for separating and detecting AuNPs involved expensive instrumentation (i.e., field-flow fractionation [7], size exclusion chromatography [8], graphite furnace atomic absorption spectroscopy [9], electrothermal atomic absorption spectrometry [10], inductively coupled plasma mass spectrometry (ICPMS) [11]) with tedious enrichment steps (i.e. liquid-liquid and solid phase extractions, cloud point extraction (CPE) [10]) or disintegration of the sample (i.e., enzymatic digestion [12,13]). No digestion of AuNPs were required in a reported method [14] in which an elaborated NPs (Al^{3+}-immobilized Fe_3O_4@silica@iminodiacetic acid) were used as sorbent materials for magnetic SPE to avoid gold ion interferences by ICPMS. Resins like Amberlite were also used for selective extracting plasmonic NPs via electrostatic interactions [9], being their elution easily performed with formic acid (8%) in methanol.

On the contrary of these expensive methods, the optical properties (fluorescence, absorbance, scattering) of NPs have been also explored for AuNP monitoring using inexpensive optical instrumentation like fluorescence [15] and especially UV spectrometer [16–19] by using

Abbreviations: AuNPs, gold nanoparticles; AgNPs, silver nanoparticles; CAPS, 3-(cyclohexylamino)-1-propanesulfonic acid; CTAC, hexadecyltrimethylammonium chloride; CTAB, hexadecyltrimethylammonium bromide; EC, capillary electrophoresis; LVSS, large-volume sample stacking; ICPMS, inductively coupled plasma mass spectrometry; TA, thiotic acid; NC, nanocellulose; NPs, nanoparticles; SDS, sodium dodecyl sulfate; SPR, surface plasmon resonance.

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Promising Sensing Platforms Based on Nanocellulose

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Abstract Nanocelluloses, typically categorized into bacterial cellulose, crystalline nanocellulose, and cellulose nanofibers, are green lightweight materials with amazing properties that are emerging in modern technology as a result of their abundance, low toxicity, large surface area, and renewability. They already have shown great promise in a myriad of uses such as reinforcing agents, templates for tridimensional ordered architectures, rheological modifiers, emulsion stabilizers, and crystallization media. However, their outstanding properties and easy-to-modulate capabilities are opening new ways of applicability in the fields of medicine, forensic and food safety analyses, environmental protection, and energy storage among others. Although applications of NC are increasing over the years, there is still plenty to discover about their capabilities of such abundant nanoscale source. This chapter briefly reviews the most promising recent approaches in sensing applications, showing the advantages of each type of NC used. It is highlighted the diverse configurations of NC (as nanopowders, films, hydrogels, aerogels) found in the recent advances, mentioning their potential characteristics offered as well as the sensing mechanisms given (colorimetric, photoluminescence, mechanical deformation, and/or electrical responses). On track for a sustainable future, the complete replacement of plastics by NC is imminently owed to the great versatility, biocompatibility, abundance, degradability, and low cost of cellulose nanomaterials. Finally, an outlook on the future perspectives for filaments and paper-based and gel-like sensing platforms of NC is given in this chapter.

Keywords Chemical stimuli, Physical stimuli, Sensors

Contents

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7.

Comunicaciones presentadas en congresos

Se han realizado un total de 14 contribuciones a 12 congresos científicos (7 nacionales y 5 internacionales), donde se han expuesto los resultados derivados de las investigaciones realizadas en esta Tesis. Cinco se presentaron como comunicación oral (tres de ellas internacionales) y nueve como comunicación tipo póster.

A continuación, se exponen por orden cronológico:

1. Screening of color developers (bisphenol A alternatives) in thermal paper and indoor dust. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada como comunicación oral en International Symposium on Halogenated Persistent Organic Pollutants (POPs) (Dioxin 2018). Celebrado en Polonia durante los días 26 - 31 de agosto de 2018.

2. Microextracción con disolventes supramoleculares de nuevos análogos de bisfenol A en muestras de polvo. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en la Séptima Edición del Encuentro sobre Nanociencia y Nanotecnología de Investigadores y Tecnólogos Andaluces (NANOUCO VII). Celebrado en Córdoba durante los días 21 y 22 de enero de 2019.

3. Analysis of emerging bisphenol A replacements (colour developers) in indoor dust from public environments. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada como comunicación oral en la 17th International Conference on Chemistry and the Environment (ICCE 2019). Celebrado en Tesalónica (Grecia) durante los días 16 - 20 de junio de 2019.

4. Microextracción de bisfenol A y análogos en muestras de polvo procedentes de diferentes microambientes utilizando disolventes supramoleculares. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en la XXII Reunión de la Sociedad Española de Química Analítica (SEQA 2019). Celebrada en Valladolid durante los días17-19 de julio de 2019.

5. Microextracción de bisfenol A y análogos emergentes de muestras de polvo utilizando un método basado en el uso de disolventes supramoleculares Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en el VIII Congreso Científico de Investigadores en Formación de la Universidad de Córdoba. Celebrado en Córdoba durante los días 18 y 19 de febrero de 2020.

6. Microextracción con disolventes supramoleculares de retardantes de llama de organofosforados en polvo procedentes de casas y centros educativos. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada como comunicación oral en el IX Congreso Científico de Investigadores en Formación de la Universidad de Córdoba. Celebrado en Córdoba (online) durante los días 3-6 de mayo de 2021.

7. Supramolecular solvent-based microextraction of oxy-PAHs from food. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en el 23rd International Symposium on Advances in Extraction Technologies (ExTech XXIII). Celebrado en Alicante (online) durante los días 30 de junio al 2 de julio de 2021.

8. Supramolecular solvent-based microextraction probe for fast detection of bisphenols by ambient mass spectrometry. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en el 23rd International Symposium on Advances in Extraction Technologies (ExTech XXIII). Celebrado en Alicante (online) durante los días 30 de junio al 2 de julio de 2021.

9. Espectrometría de masas ambiental con SUPRAS contenidos en sondas para la detección rápida de contaminantes en materiales. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada como comunicación oral en la X Reunión de la Sociedad Española de Espectrometría de Masas (X-RSEEM). Celebrado en Córdoba durante los días 1-3 de junio de 2022.

10. Microextracción con SUPRAS previo a análisis por ASAP-MS/MS para la determinación de contaminantes de envases de alimentos. Autores: **M. J. Dueñas-Mas**, Cristina de Dios-Pérez, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en la X Reunión de la Sociedad Española de Espectrometría de Masas (X-RSEEM). Celebrado en Córdoba durante los días 1-3 de junio de 2022.

11. Microextracción con disolventes supramoleculares (SUPRAS) contenidos en sondas de vidrio para la detección ultrarrápida de

bisfenoles mediante espectrometría de masas ambiental. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en la XXIII Reunión de la Sociedad Española de Química Analítica (SEQA 2022). Celebrada en Oviedo durante los días 12-15 de julio de 2022.

12. Determination of per- and polyfluoroalkyl substances (pfas) and polyfluoroalkyl phosphate esters (paps) in food packaging material by LC-MS. Autores: J. de Boer, **M.J. Dueñas-Mas**. Presentada como comunicación oral en la International Mass Spectrometry Conference (IMSC 2022). Celebrada en Maastricht (Países Bajos) entre los días 27 Agosto 2023 – 1 de Septiembre 2023.

13. De una hora a un minuto: detección rápida de bisfenoles en papel térmico mediante el uso de espectrometría de masas ambiental con SUPRAS contenidos en capilares de vidrio. Autores: **M. J. Dueñas-Mas**, A. Ballesteros-Gómez, S. Rubio. Presentada en formato póster en la XVII Reunión del Grupo Regional Andaluz de la Sociedad Española de Química Analítica (GRASEQA 2022). Celebrada en Sevilla durante los días 6 y 7 de octubre de 2022.

14. Comparative chemical profiling of underexploited Citrus sinensis I. Herbal dust extracts obtained by subcritical water and pressurized ethanol extractions. Autores: S. Krivosija; A. Ballesteros-Gómez, M. J. Dueñas-Mas, M. Tomic, N. Nastic, M. Sulejmanovic, S. Vidovic. Presentada en formato póster en la 2nd Greenering International Conference. Celebrada en Valladolid entre los días 21 – 23 Marzo 2023.

100th Anniversary of the Regaining Independence by Poland

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Screening of color developers (bisphenol A alternatives) in thermal paper and indoor dust

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Introduction: The chemical safety of consumer products is an issue of emerging concern. Thermal paper contains potentially toxic additives, such as bisphenol A (BPA), as a common color developer. Because of its known endocrine disrupting effects, structural analogues to BPA such as bisphenol S (BPS) have been used as replacements, but still little is known about the presence and toxicological effects of these compounds. The presence of BPA and replacements was investigated in thermal paper and in indoor dust.

Materials and Methods: thermal paper samples were collected in European countries (Netherlands, Spain, Sweden and Norway) in 2015 and 2016. A variety of cash receipts and other thermal paper products (n = 141, cinema tickets, boarding passes and luggage tags) were analyzed. Indoor dust samples (n = 20) as a common route for human exposure to organic contaminants (via inhalation or ingestion) were collected in Spain in 2018. Samples were collected in bedrooms, offices, cars and shops. Novel extraction and detection methods were employed for the screening of developers and aimed to cover a wide range of contaminants and to operate in an easy and fast way. Suspect and non-target screening was carried out, the former based on the list of candidates of the EPA 2015 report [1]. Thermal paper was directly screened by direct probe ambient mass spectrometry (rapid pre-screening method not requiring sample preparation) with high resolution time-of flight mass spectrometry (TOF-MS) and results subsequently confirmed by standard liquid chromatography (LC) and TOF-MS. Glass probes were loaded with a small amount of sample (few mg) by scratching the surface of the paper and directly injected onto the direct probe-APCI ambient MS source. Regarding indoor dust samples, a novel supramolecular solvent (SUPRAS) method was employed for sample preparation (liquid-liquid microextraction and simultaneous clean-up). SUPRAS are nanostructured liquids made up by self-assembled amphiphilic compounds, in our case by a long chain alkanediol in mixtures of tetrahydrofuran : water. These multi-target extractants are very suitable for screening and can be applied to a wide polarity range of compounds. SUPRAS also have restricted access properties, due to the limited size of the ¨pores¨ of the nanonetwork, so that common interferents (macromolecules as proteins, polymers or humic acids) can be excluded.

Results: Bisphenol A, Bisphenol S, Pergafast 201, D-8, D-90 and TGSA were present with detection frequencies (%) of 63, 56, 23, 10, 10 and 8, respectively, in cash receipts. Besides the already reported BPA and BPS, other developers only recently reported in paper (Pergafast 201, D-8) or to the best of our knowledge not reported before (D-90, TGSA, BPS-MAE) were frequently found as well as some related unreported impurities. Some of these novel compounds were also frequently present in indoor dust, so that together with BPA and BPS, we found TGSA, BPS-MAE and D-8. We suspect other widespread use different than in thermal paper of some them due to their ubiquity and presence in procedurals blanks. TGSA and D-8 are labelled as toxic to the aquatic environment (EU) while BPS-MAE is considered as very toxic. In general, there is a lack of environmental and toxicity data about these compounds.

Acknowledgements: ABG acknowledges the funding by the Spanish Ministry of Economy, Industry and Competitiveness (MINECO) for a Ramon y Cajal contract (RYC-2015-18482).

References:
[1]US EPA, 2015. Bisphenol A alternatives in thermal paper, final report.

Abstracts Book of the Dioxin 2018 : 38th International Symposium on Halogenated Persistent Organic Pollutants & 10th International PCB Workshop, 26-31 August 2018, Kraków, Poland

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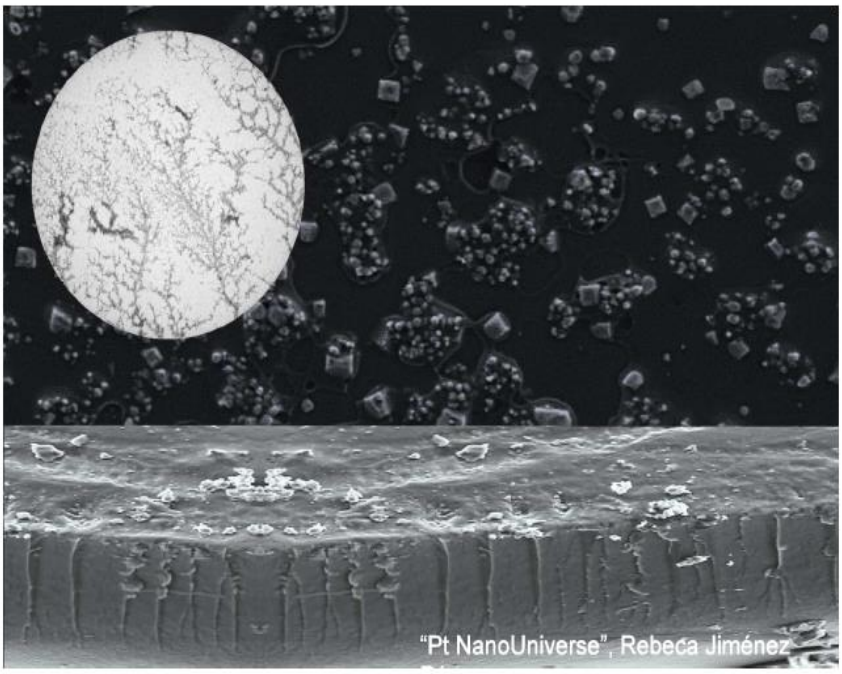

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P45-CA

MICROEXTRACCIÓN CON DISOLVENTES SUPRAMOLECULARES DE NUEVOS ANÁLOGOS DE BISFENOL A EN MUESTRAS DE POLVO

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El Bisfenol A (BPA) es un compuesto usado en una amplia variedad de materiales, por lo que se encuentra de manera generalizada en el medio ambiente. Por esta razón, la industria ha introducido varios análogos como el Bisfenol S o el Bisfenol F, y otros menos conocidos, como el BPS-MAE, D8 o TGSA, los cuales han sido recientemente identificados por nuestro grupo de investigación en papel térmico [1]. La potencial toxicidad de estos nuevos contaminantes y su migración al ambiente aún no han sido investigadas.

En este trabajo, se ha optimizado un método de microextracción basado en disolventes supramoleculares (SUPRAS) para la extracción del BPA y sus análogos en muestras de polvo recogidas en diferentes microambientes. En concreto se recogieron muestras de tiendas, debido al uso frecuente de tickets de papel térmico en estos lugares, así como de oficinas, habitaciones y comedores de casas y coches, con el fin de determinar si los nuevos sustitutos de BPA tienen un amplio uso en otro tipo de productos, así como su capacidad de migración. El polvo doméstico ha sido reconocido como una de las fuentes principales de exposición humana a contaminantes a través de contacto dérmico o inhalación e ingestión y es una matriz compleja de muy diversa composición. En este sentido, los SUPRAS ofrecen una alternativa interesante para el desarrollo de métodos simples y rápidos, con bajo consumo de reactivos, que permiten realizar la etapa de extracción y *clean-up* de manera simultánea. Además, los SUPRAS ofrecen múltiples interacciones y sitios de unión para la extracción de compuestos en una amplia polaridad, propiedades clave para el desarrollo de métodos de preparación de muestra genéricos y adaptables a una amplia diversidad de matrices complejas tales como el polvo. Un total de 62 muestras (25 mg) fueron analizadas en microtubos de 2 mL, tras la adición de la solución de síntesis de SUPRAS (200 μL hexanol, 200 μL THF, 800 μL agua) y de estándares internos (BPA-d6 and BPS-d8), extracción con vórtex (5 min), centrifugación (20 min) y posterior análisis por LC-MS/MS. BPS-MAE, D8 y TGSA fueron detectados por primera vez en muestras de polvo en un intervalo de concentraciones medianas de n.d. – 325 $ng \cdot g^{-1}$, 8 – 145 $ng \cdot g^{-1}$ y 7 – 91 $ng \cdot g^{-1}$, respectivamente, con porcentajes de detección comprendidos entre n.d – 50%, 12 – 70% y 69 – 90%, respectivamente, y sin diferencias significativas entre microambientes. Estos resultados reflejan la capacidad que tienen estos compuestos de migrar al medio ambiente, y su presencia en otros microambientes como habitaciones, salones o coches, demuestra que su procedencia no es exclusivamente del papel térmico.

Agradecimientos: Los autores agradecen el apoyo financiero del Ministerio Español de Ciencia, Innovación y Universidades (Proyecto CTQ2017-83823R). A.B.G agradece su beca Ramón y Cajal (RYC-2015-18482)

1. Björnsdotter, M.K.; Jonker, W.; Legradi, J.; Kool, J.; and Ballesteros-Gómez, A. 2017. Bisphenol A alternatives in thermal paper from the Netherlands, Spain, Sweden and Norway. Screening and potential toxicity. *Science of the Total Environment* 601–602, 210–221. Doi: 10.1016/j.scitotenv.2017.05.171.

CONFERENCE PROCEEDINGS

Analysis of emerging bisphenol A replacements (colour developers) in indoor dust from public environments

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Abstract

Bisphenol A (BPA) is present in a wide variety of materials and it is a well-known endocrine disruptor that is widespread in indoor and outdoor environments. In order to evade regulatory oversight and social pressure, industry has introduced BPA replacements into the market. Replacements are usually structural analogs to BPA with similar physicochemical properties and, subsequently, similar potential toxicity. Bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol AF (BPAF), bisphenol E (BPE), tetrabromobisphenol A (TBBPA), bisphenol A diglycidyl ether (BADGE) and bisphenol F diglycidyl ether (BFDGE) are common BPA replacements. They are used in a variety of materials too, such as electronic equipment, cans' lacquer coating, dental sealants and flame retarded products and have also been widely reported in environmental and biological samples. Other widespread use of BPA is thermal paper (Geens et al., 2012; ,Björnsdotter et al., 2017a). Replacements have also been introduced into the market for this aim, namely BPS and other less known compounds such as 4-hydroxyphenyl 4-isopropoxyphenyl Sulfone (D-8), 4,4′-sulfonylbis(2-allylphenol) (TGSA), 4-((4-(allyloxy)phenyl)sulfonyl)phenol (BPS-MAE), Pergafast 201 and D-90 (US EPA, 2015). Although there are some recent studies about the presence of these compounds in thermal paper products and their potential toxic effects (Goldinger et al. 2015; Björnsdotter et al., 2017b) their migration and presence in the environment have not been assessed so far.

In the present study, BPA replacements used in thermal paper (BPF, BPS, BPS-MAE, D-8, TGSA) were analyzed in indoor dust. Indoor dust is a potential source of human exposure to BPA and its analogs due to their migration from many materials and slow degradation. Concentration values of BPA and PBS in indoor dust usually range from $ng \cdot g^{-1}$ to $\mu g \cdot g^{-1}$ levels. We optimized a novel supramolecular solvent (SUPRAS)-based microextraction method for the analysis of BP replacements in indoor dust. SUPRAS are multi-target nanostructured solvents made up of self-assembled amphiphiles. They offer multiple extraction interactions (dispersion, polar, hydrophobic, etc.) and they constitute excellent candidates to develop generic and fast sample treatment procedures at low cost. These properties make them excellent candidates for generic sample treatment of indoor dust, a complex and heterogeneous matrix containing from textile and paper fibers to human or animal hair, cells and mineral components, among others. Dust samples were collected in public environments, because of the frequent use of thermal paper cash receipts and in other type of indoor environments (houses, cars, offices and bedrooms). Sampling was performed using a vacuum cleaner with bags. Dust samples were collected in Spain in 2018 from public environments (n=57). They were homogenized and sieved to 0.5 mm. BPA, BPS, BPF, D-8, TGSA and BPS-MAE were determined by SUPRAS (sample preparation) and LC-MS/MS.

Keywords: supramolecular solvents, indoor dust, bisphenol A, bisphenol S, BPS-MAE, D-8, TGSA

Tables and Figures

For sample preparation with SUPRAS, aliquots of 25 mg of dust were weighed in 2 mL Eppendorf microtubes. The SUPRAS synthetic solution (200 µL of hexanol, 200 µL of THF and 800 µL of water) was added and spiked with 25µL of IS mix. SUPRAS formation and microextraction/clean-up was performed in a single-step by vortexing (5 min) and centrifugation at 10,000 rpm for 20 min. After phase-separation, 150 µL of SUPRAS (the top layer) was collected, transferred to an LC vial and aliquots of 3 µL measured by LC MS/MS. A schema is shown in Figure 1.Recoveries were within the required levels (69 – 108%) and LODs were satisfactory for this matrix (in the low $ng \cdot g^{-1}$).

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MICROEXTRACCIÓN DE BISFENOL A Y ANÁLOGOS EN MUESTRAS DE POLVO PROCEDENTES DE DIFERENTES MICROAMBIENTES UTILIZANDO DISOLVENTES SUPRAMOLECULARES

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El bisfenol A (BPA) es un compuesto empleado en una amplia variedad de materiales. Debido a su toxicidad y capacidad de migración al medio ambiente, la industria ha introducido numerosos sustitutos, de los cuales algunos se utilizan ampliamente (ej. bisfenol S y bisfenol F) y su toxicidad y presencia en el ambiente está muy documentada. Otros sustitutos del BPA como 4-hydroxyphenyl 4-isopropoxyphenyl sulfone (D-8), el 4,4′-sulfonylbis(2-allylphenol) (TGSA) o el 4-((4-(allyloxy)phenyl)sulfonyl)phenol (BPS-MAE) han sido escasamente investigados pero su presencia en papel térmico se ha detectado en estudios recientes [1]. La peligrosidad y capacidad de migración al medio de estos compuestos aún no se ha documentado. Dado que el polvo es considerado una importante fuente de exposición a contaminantes orgánicos, se ha seleccionado en esta investigación como matriz de referencia para evaluar la migración de estos nuevos compuestos al ambiente.

El objetivo de este trabajo ha sido la optimización un método para la microextracción de D-8, TGSA y BPS-MAE en muestras de polvo basado en el uso de disolventes supramoleculares (SUPRAS). Los SUPRAS son disolventes nanoestructurados constituidos por ensamblaje de moléculas anfifílicas. Los SUPRAS ofrecen múltiples sitios de unión para la extracción de compuestos de diferente polaridad y exclusión simultánea de macromoléculas, además de favorecer el desarrollo de métodos con bajo consumo de reactivos, simples y rápidos (ya que la etapa de extracción y *clean-up* ocurren simultáneamente). Estas propiedades hacen de los SUPRAS extractantes idóneos para matrices complejas como el polvo doméstico.

Las muestras de polvo analizadas se recogieron en diferentes microambientes en Córdoba, tales como tiendas y otros lugares públicos (donde el uso de papel térmico es frecuente), así como en habitaciones y salones de casas, coches y oficinas. Se analizaron un total de 57 muestras recogidas entre 2017 y 2018. Se tomaron alícuotas de 25 mg (tamizadas con una luz de malla de 0.5 mm) en microcrotubos de 2 mL, donde posteriormente se añadieron el anfifilo y los ingredientes para la formación del SUPRAS (200 μL 1-hexanol, 200 μL THF y 800 μL agua) y una mezcla de estándares internos (BPA-d6 y BPS-d8). A continuación, se agitaron las muestras con vórtex (5 minutos, 3,000 rpm) para favorecer la formación del SUPRAS y la extracción y *clean-up* simultáneos y se centrifugaron (20 minutos, 10,000 rpm) para acelerar la separación de fases. Se analizó la fase superior (SUPRAS con los analitos de interés) mediante LC-MS/MS. Los nuevos sustitutos de BPA (BPS-MAE, D8 y TGSA) se detectaron en un intervalo de concentraciones medias de 20 – 325 $ng \cdot g^{-1}$, 8 – 36 $ng \cdot g^{-1}$ y 7 – 89 $ng \cdot g^{-1}$ y porcentajes de detección comprendidos entre 0 – 55%, 6 – 70% y 69 – 82%, respectivamente, y sin diferencias significativas entre microambientes. Estos resultados reflejan la capacidad que tienen estos compuestos de migrar al medio ambiente. Su presencia en microambientes como habitaciones, salones o coches, demuestra que su procedencia no es exclusivamente del papel térmico.

Agradecimientos: Los autores agradecen el apoyo financiero del Ministerio Español de Ciencia, Innovación y Universidades (Proyecto CTQ2017-83823R). A.B.G agradece su beca Ramón y Cajal (RYC-2015-18482).

[1] M.K. Björnsdotter, W. Jonker, J. Legradi, J. Kool y A. Ballesteros-Gómez, Sci. Total Environ. 601–602 (2017) 210–221

Microextracción de bisfenol A y análogos emergentes de muestras de polvo utilizando un método basado en el uso de disolventes supramoleculares

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Summary

Bisphenol A (BPA) is a compound largely used by industry in a wide range of materials, and consequently, it is widely present in the environment. Due to its toxicity and migration capacity, new substitutes were introduced into the market, such as bisphenol S (BPS) and bisphenol F (BPF), and other less-known as BPS-MAE, D8 or TGSA, which little is known about their toxicity and migration to the environment. All of them have been recently detected in thermal paper by our group, so in this study we have optimized a supramolecular solvent-based microextraction method to extract these compounds in dust samples from different microenvironments, such as shops (because of the wide use of tickets of thermal paper in these areas) and other places as offices, cars and bedrooms and living rooms from houses, in order to investigate their possible use in other materials different from thermal paper and their possible migration.

Resumen

El Bisfenol A (BPA) es un compuesto ampliamente utilizado por la industria para la fabricación de diversos materiales, por lo que se encuentra de manera generalizada en el medio ambiente. Debido a su toxicidad y presencia en el medio, comenzaron a utilizarse otros compuestos análogos, tales como el Bisfenol S o el Bisfenol F, y posteriormente, otros menos conocidos, como el BPS-MAE, D8 o TGSA, de los cuales se conoce poco acerca de su toxicidad y migración al ambiente. Todos ellos han sido detectados recientemente en papel térmico por nuestro grupo, por lo que en este estudio se ha optimizado un método de microextracción basado en disolventes supramoleculares para la extracción de estos compuestos en muestras de polvo recogidas en diferentes microambientes, tales como tiendas (debido al abundante uso de los tickets de papel térmico en dichos lugares) y otros como oficinas, coches y habitaciones y salones de casas, con el fin de investigar su posible uso en otros materiales diferentes del papel térmico y su posible migración.


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Ciencias

Microextracción con disolventes supramoleculares de retardantes de llama organofosforados en polvo procedente de casas y centros educativos en España

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Summary

Aryl-phosphate flame retardants (aryl-OPFRs) are flame retardants that can be found in a wide variety of products, from furniture and textiles to cars and electronic equipment. Due to their ubiquity and potential toxicity, there is an increasing concern about the human exposure to these contaminants, because of as additives, they can be easily released to the environment. In this study, we investigated the presence of six representative aryl-OPFRs, two well-known aryl-OPFRs (triphenyl phosphate, TPHP and 2- ethylhexyl diphenyl phosphate, EHDPP), two novel aryl-OPFRs (cresyl diphenyl phosphate, CDP and isodecyl diphenyl phosphate, IDPP) and two oligomeric aryl-OPFRs [bisphenol A bis (diphenyl phosphate), BDP and resorcinol bis(diphenyl phosphate, RDP] in indoor dust from houses and education buildings from Spain. A simple and rapid extraction method was developed, based on supramolecular solvents (SUPRAS) prior to LCMS/ MS analysis. The median Σaryl-OPFRs was two times higher in classrooms than in houses, being particularly high at University classrooms. The most abundant aryl-OPFR in houses was TPHP (median 497 $ng \cdot g^{-1}$) while EHDPP (median 407 $ng \cdot g^{-1}$) and IDPP (median 403 $ng \cdot g^{-1}$) were dominant in classrooms. This is the first study reporting IDPP, BDP and RDP in different education buildings.

Key words: flame retardants, aryl-phosphates, indoor dust.

Resumen

Los retardantes de llama organofosforados con sustituyentes arilo (aril-OPFRs) son compuestos que pueden encontrarse en una amplia variedad de productos, desde muebles y textiles, a coches y equipos electrónicos. Debido a su ubicuidad y potencial toxicidad, existe una creciente preocupación sobre la exposición humana a estos contaminantes, ya que al ser aditivos, pueden migrar fácilmente del producto al ambiente. En este estudio, se han investigado la presencia de 6

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BOOK OF ABSTRACTS

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SUPRAMOLECULAR SOLVENT-BASED MICROEXTRACTION OF OXY-PAHS FROM FOOD

María Jesús Dueñas-Mas[1*], Ana Ballesteros-Gómez[1], Soledad Rubio[1]

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Supramolecular solvents (SUPRAS) are nanostructured liquids formed by the self-assembly of amphiphilic aggregates with multiple binding sites and microenvironments of different polarity for efficient extraction at low volumes. [1] In this study, we have investigated the suitability of supramolecular solvents (SUPRAS)-based microextraction for the development of generic and fast sample treatment of solid foods prior liquid chromatography and high resolution mass spectrometry (LC-MS-QTOF) for the determination of oxygenated PAHs (oxy-PAHs). Oxy-PAHs have been scarcely studied in food despite the growing concern about their presence in these matrices due to their toxicity. In order to provide a green extraction method, the SUPRAS was made up of short/medium chain length alcohols (C_6-C_{10}) in mixtures of water and a sustainable solvent (methyl-tetrahydrofuran). These amphiphilic compounds of low toxicity and volatility are approved for use in food and cosmetics. The following variables were optimized in term of extraction efficiency and matrix effects: alcohol chain length and organic solvent percentage for SUPRAS production and sample amount. Mussels and chicken samples were used for optimization and validation. Total recoveries varied in the range 94-108% (RSD:7-14%) for mussels and between 89 and 95% (RSD: 3-12%) for chicken. The method provided quantification limits of 3 ng/g with low consumption of reagents (200uL of SUPRAS per sample) and it was based on simple agitation and centrifugation steps without concentration/evaporation. It was applied to several meat and fish-based processed food bought in local supermarkets in Spain. Low contamination levels (few ng/g) of oxy-PAHs were found in samples in a range 3 – 7.3 ng/g.

Acknowledgements:
This work was supported by Spanish Ministry of Science, Innovation and Universities (fellowships RYC-2015-18482, PRE2018-083336) and the Andalusian Government (Project P18-RT-2654).

References:

[1] E. Romera-García, A. Ballesteros-Gómez, Supramolecular Solvents in the Analytical Process. In Encyclopedia of Analytical Chemistry, R.A. Meyers (Ed.) (2020)

P165

SUPRAMOLECULAR SOLVENT-BASED MICROEXTRACTION PROBE FOR FAST DETECTION OF BISPHENOLS BY AMBIENT MASS SPECTROMETRY

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Ambient mass spectrometry (AMS) has emerged as promising techniques for fast screening of organic compounds. AMS consists in modified atmospheric pressure ionization sources, where solid o liquid samples are directly introduced (without previous preparation or chromatography separation) so that analytes desorb from the matrix and enter the MS detector.[1] In this study we investigated the suitability of supramolecular solvent(SUPRAS)-based microextraction probe for the development of generic and fast sample treatment prior to AMS analysis based on ASAP (atmospheric solids analysis probe). SUPRAS are nanostructured liquids formed by the self-assembly of amphiphilic aggregates with multiple binding sites and microenvironments of different polarity for efficient extraction at low volumes. [2] In ASAP, the solid or liquid sample is directly injected on disposable glass probes onto a modified atmospheric pressure chemical ionization (APCI) source. SUPRAS made up of fatty alcohols of different chain length (C6-C10) in mixtures of water and ethanol or tetrahydrofuran were tested to improve the sensitivity and selectivity of ASAP, to generate reproducible and integrable signals for data processing and to reduce cross-contamination. All these aspects are crucial to extent the applicability of AMS to routine analysis. The method was applied to the screening of bisphenol A and six structural analogues in thermal paper and food contact materials. Optimal results were achieved with SUPRAS synthesized with 1-decanol in mixtures of ethanol: water. SUPRAS (0.5-2 µL) were loaded onto glass probes that were placed in contact with samples for 5 seconds before ASAP analysis. AMS integrable peaks (0.2-0.5 min) were obtained with relative standard deviations of 2-25%. The method was applied to 62 samples of thermal paper and 14 samples of food containers from Spain. The results showed that BPA and BPS were the most widely used bisphenols in thermal paper and BPS in food packaging products, which suggests the increasing industrial replacement of BPA by BPS.

Acknowledgements:
This work was supported by Spanish Ministry of Science, Innovation and Universities (Project CTQ2017-83823R, RYC-2015-18482, PRE2018-083336).

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[1] M. Kostopoulou, A. Nikolaou, TrAC 27, 1023 (2008).
[2] E. Romera-García, A. Ballesteros-Gómez, Supramolecular Solvents in the Analytical Process. In Encyclopedia of Analytical Chemistry, R.A. Meyers (Ed.) (2020).


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Comunicaciones Orales
Sesión 1: Medio Ambiente (I) 01/06/2022

O-1. Espectrometría de masas ambiental con SUPRAS contenidos en sondas para la detección rápida de contaminantes en materiales

María Jesús Dueñas Mas[1], Ana María Ballesteros-Gómez[1], Soledad Rubio Bravo[1]
1 Universidad de Córdoba, Córdoba

Área: Medio Ambiente
Tipo Comunicación: XRSEEM ORAL
Palabras Clave: Espectrometría de masas ambiental, ASAP, SUPRAS, bisfenoles, papel térmico

RESUMEN:
En este estudio, se investiga el empleo de sondas de microextracción con disolventes supramoleculares (SUPRAS) para el desarrollo de tratamientos rápidos y genéricos de muestra previos a análisis cualitativo mediante espectrometría de masas ambiental basada en ASAP (atmospheric solids analysis probe).
La espectrometría de masas ambiental consiste en la introducción directa de la muestra en el analizador. La técnica ASAP consiste en colocar la muestra en un capilar de vidrio que es introducido directamente en la fuente APCI, donde los analitos son desorbidos por temperatura e ionizados por la corona de descarga. El número de estudios acerca de estrategias de preparación de muestras acopladas a la espectrometría de masas ambiental está aumentando rápidamente con el objetivo de mejorar la reproducibilidad, selectividad y sensibilidad de estas técnicas. Los SUPRAS son líquidos nanoestructurados formados por el autoensamblaje de agregados anfifílicos con múltiples sitios de unión y microambientes de diferente polaridad, lo que los convierte en excelentes extractantes.
Con el fin de proponer una etapa de tratamiento de muestra simple y rápida, los SUPRAS fueron cargados en sondas de vidrio de ASAP (1,1?2 ?L) y se pusieron en contacto con las muestras durante 10 s antes del análisis. Se evaluaron diferentes tipos de SUPRAS de agregados inversos preparados con agua, distintos disolvente orgánicos y distintos anfifilos (ácidos carboxílicos, alcoholes y dioles, C6-C10). El método se aplicó al cribado de bisfenol A y análogos en papel térmico. Los resultados óptimos se lograron con SUPRAS de 1-decanol en mezclas de etanol:agua. Los picos de señal de AMS (ancho: 0,2?0,5 min) se integraron y normalizaron fácilmente con estándares internos (RSD: 2?25 %). Por el contrario, el análisis directo de sólidos generó una señal de MS continua y contaminación cruzada en la fuente debido a la liberación de partículas. Se analizaron 62 muestras (tickets de supermercados, tiendas, gasolineras, etc.). El BPA y el BPS fueron los más utilizados, lo que pone de manifiesto la progresiva sustitución industrial del BPA por el BPS. El uso de otras alternativas (TGSA, Pergafast 201, D-8, etc.) es aún es limitado.

P-1. Microextracción con SUPRAS previo a análisis por ASAP-MS/MS para la determinación de contaminantes en envases de alimentos

Cristina de Dios Pérez[1], María Jesús Dueñas Mas[1], Ana María Ballesteros Gómez[1], Soledad Rubio[1]
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Área: Medio Ambiente
Tipo Comunicación: XRSEEM POSTER
Palabras Clave: Espectrometría de masas ambiental, ASAP, SUPRAS, bisfenoles, retardantes de llama, envases.

RESUMEN:
En este estudio se desarrolló un método rápido de detección y cuantificación de contaminantes orgánicos en envases de alimentos que consistió en una microextracción rápida con disolventes supramoleculares (SUPRAS) y análisis mediante espectrometría de masas ambiental basada en ASAP (Atmospheric Solids Analysis Probe). Esta técnica emplea capilares de vidrio donde se carga la muestra y se introducen directamente en una fuente de ionización de tipo APCI, en la cual se produce la desorción térmica de los analitos y su ionización mediante la corona de descarga.

Los SUPRAS son líquidos nanoestructurados formados por el autoensamblaje de agregados anfifílicos con múltiples sitios de unión y microambientes de diferente polaridad, lo que los convierte en excelentes extractantes. Con el fin de proponer una etapa de tratamiento de muestra simple y rápida para la determinación de contaminantes en materiales con ASAP se optimizó una extracción empleando 400 µL de SUPRAS de agregados inversos de 1-decanol en mezclas etanol:agua y 20 mg de muestra, que se sometieron a agitación (1 minuto en vórtex) y posterior centrifugación. A continuación el extracto fue cargado en las sondas de vidrio de ASAP y analizado por esta técnica para obtener resultados cualitativos y cuantitativos. Se analizaron un total de 40 muestras procedentes de envases de alimentos adquiridos en supermercados locales. La combinación de ASAP con un detector de masas de triple cuadrupolo (MS/MS) permitió la cuantificación sensible (LODs: 0.02-1 µg/g) y reproducible (?20%) de bisfenol A y 5 derivados y de 6 retardantes de llama organofosforados. BPA y BPS fueron los analitos predominantes en los envases y en menor frecuencia se hallaron los retardantes de llama EHDPP y CDP. El empleo de ASAP con un detector de masas de alta resolución (QTOF) y la búsqueda en librerías espectrales permitió llevar a cabo un cribado no dirigido identificando 17 compuestos de (4 de origen vegetal procedentes del alimento), 8 aditivos plásticos (filtros UV, ácidos grasos y ftalatos) y 5 de uso no identificado. Los resultados mostraron que las muestras de envases son complejas y que alrededor de la mitad contuvieron bisfenoles o retardantes de llama, así como otros aditivos y compuestos desconocidos, siendo una vía de exposición a contaminantes emergentes relevante para la salud.

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P179

Microextracción con disolventes supramoleculares (SUPRAS) contenidos en sondas de vidrio para la detección ultrarrápida de bisfenoles mediante espectrometría de masas ambiental

María Jesús Dueñas Mas, Ana María Ballesteros-Gómez, Soledad Rubio-Bravo.

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En este estudio, se investiga el empleo de sondas de microextracción con disolventes supramoleculares (SUPRAS) para el desarrollo de tratamientos rápidos y genéricos de muestra previos a análisis cualitativo mediante espectrometría de masas ambiental basada en ASAP (atmospheric solids analysis probe).
La espectrometría de masas ambiental consiste en la introducción directa de la muestra en el analizador. La técnica ASAP consiste en colocar la muestra en un capilar de vidrio que es introducido directamente en la fuente APCI, donde los analitos son desorbidos por temperatura e ionizados por la corona de descarga. El número de estudios acerca de estrategias de preparación de muestras acopladas a la espectrometría de masas ambiental está aumentando rápidamente con el objetivo de mejorar la reproducibilidad, selectividad y sensibilidad de estas técnicas.

Los SUPRAS son líquidos nanoestructurados formados por el autoensamblaje de agregados anfifílicos con múltiples sitios de unión y microambientes de diferente polaridad, lo que los convierte en excelentes extractantes.

Con el fin de proponer una etapa de tratamiento de muestra simple y rápida, los SUPRAS fueron cargados en sondas de vidrio de ASAP (1,1–2 µL) y se pusieron en contacto con las muestras durante 10 s antes del análisis. Se evaluaron diferentes tipos de SUPRAS de agregados inversos preparados con agua, distintos disolvente orgánicos y distintos anfifilos (ácidos carboxílicos, alcoholes y dioles, C6-C10). El método se aplicó al cribado de bisfenol A y análogos en papel térmico. Los resultados óptimos se lograron con SUPRAS de 1-decanol en mezclas de etanol:agua. Los picos de señal de AMS (ancho: 0,2–0,5 min) se integraron y normalizaron fácilmente con estándares internos (RSD: 2–25 %). Por el contrario, el análisis directo de sólidos generó una señal de MS continua y contaminación cruzada en la fuente debido a la liberación de partículas. Se analizaron 62 muestras (tickets de supermercados, tiendas, gasolineras, etc.). El BPA y el BPS fueron los más utilizados, lo que pone de manifiesto la progresiva sustitución industrial del BPA por el BPS. El uso de otras alternativas (TGSA, Pergafast 201, D-8, etc.) es aún es limitado.

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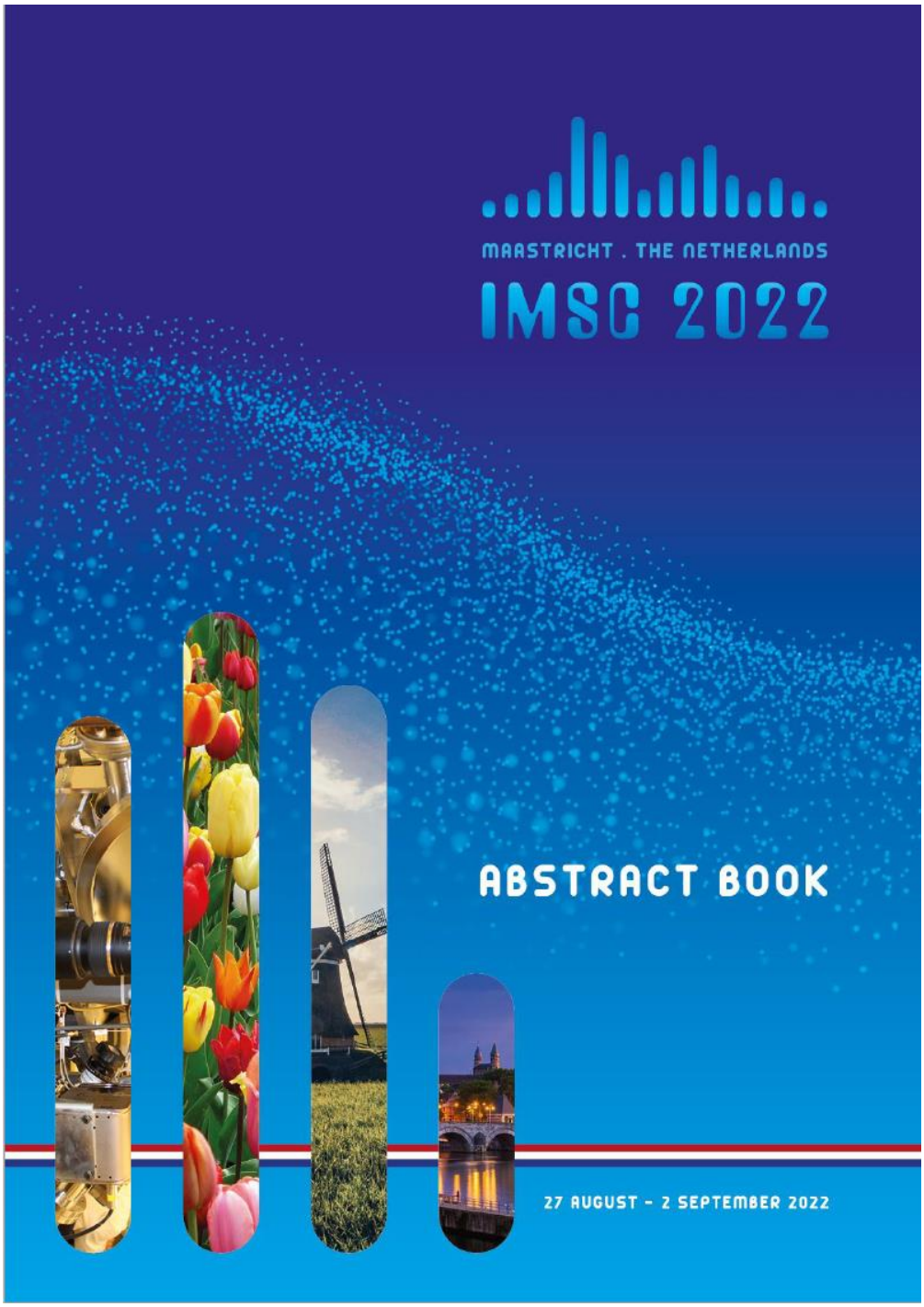
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IMSC 2022

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DETERMINATION OF PER- AND POLYFLUOROALKYL SUBSTANCES (PFAS) AND POLYFLUOROALKYL PHOSPHATE ESTERS (PAPS) IN FOOD PACKAGING MATERIAL BY LC-MS

Abstract ID: **701**

Presenting author: Jacob de Boer, Amsterdam Institute for Life and Environment, Vrije Universiteit

Introduction

Per- and polyfluroalkyl substances (PFAS) are highly fluorinated compounds. They are fat, water and dirt-repellent. Therefore, they have many useful applications. However, due to their extreme persistency, they have been detected in the environment and humans, and have been associated with different diseases. Therefore, PFAS are considered environmental pollutants of high concern. The polyfluoroalkyl phosphate esters (PAPs) have been identified as potential precursors of PFAS. Some studies have evidenced that they are more toxic than PFAS themselves. PAPs are mainly used in food packaging materials. They have also been detected in sewage sludge and human serum.

We have developed an LC/MS method for the determination of several PFAS, including PAPs, in food-contact materials.

Methods

Instrument: Bruker, ELUTE LC with a triple-quad Elite EVOQ MS, neg. ESI. Source parameters: spray voltage 4500V; cone temperature 350°C; cone gas flow 25 L/h; heated probe 375°C; probe gas flow 45 L/h; nebulizer 55 L/h. Columns: XBridge BEH C18 (150x2.1 mm, 2.5 mm), pre-column: XBridge BEH C_{18} (50x2.1 mm, 2.5 mm). Mobile phase: Milli-Q water (A) and methanol (B) both containing 0.1% NH_4OH, flow rate 0.3 ml/min. Gradient: 0.5 min 5% B, increasing to 50% (1.5 min) and to 99% (8 min), maintained 8 min, decreasing to initial conditions, 4 min.

Preliminary data (results)

NH_4OH was added to the mobile phase to increase the pH until 9, to improve the mono-PAPs peak shape. PAPs are very polar and have strong interactions with the polar part of the stationary phase. In this way, the phosphate groups are ionized and polar interactions are avoided. Figure 1A shows the differences in the TIC chromatograms with NH_4OH in the mobile phase between 0.05% and 0.1%. The best resolution was obtained with 0.1% NH_4OH, due to the higher dissociation of the phosphate group. Various flow rates were tested (0.2, 0.3 and 0.35 ml/min). Those TIC PAP chromatograms are shown in figure 1B. Due to the higher signal, a flow of 0.3 ml/min was selected above 0.35 ml/min, while a better peak resolution was obtained compared to a flow of 0.2 ml/min. Due to the low sensitivity of PAPs, pre-concentration will always be necessary. The SPE step that is already included in the method allows that. Figure 2 shows PAP chromatograms (A: TIC; B: 8:2 diPAP; C: 10:2 diPAP) with the PAPs in two different concentrations (1 and 0.01 mg/ml). In the case of 8:2 diPAP (2B) and 10:2 diPAP (2C) the signal is completely absent at low concentrations, which complicates their detection in real samples where concentrations might be very low, down to 0.1 ng/g for di-PAPs. However, we plan to use a Sciex LC/MS for the final analyses (Exion 6500+ QTRAP LC/MS, ion spray 4000V).

Please explain why your abstract is innovative for mass spectrometry?

Application of Sciex QTRAP LC/MS

Co-authors:

Maria Jesús Dueñas Mas, Department of Analytical Chemistry, Institute of Fine Chemistry and Nanochemistry, Campus of Rabanales, University of Córdoba

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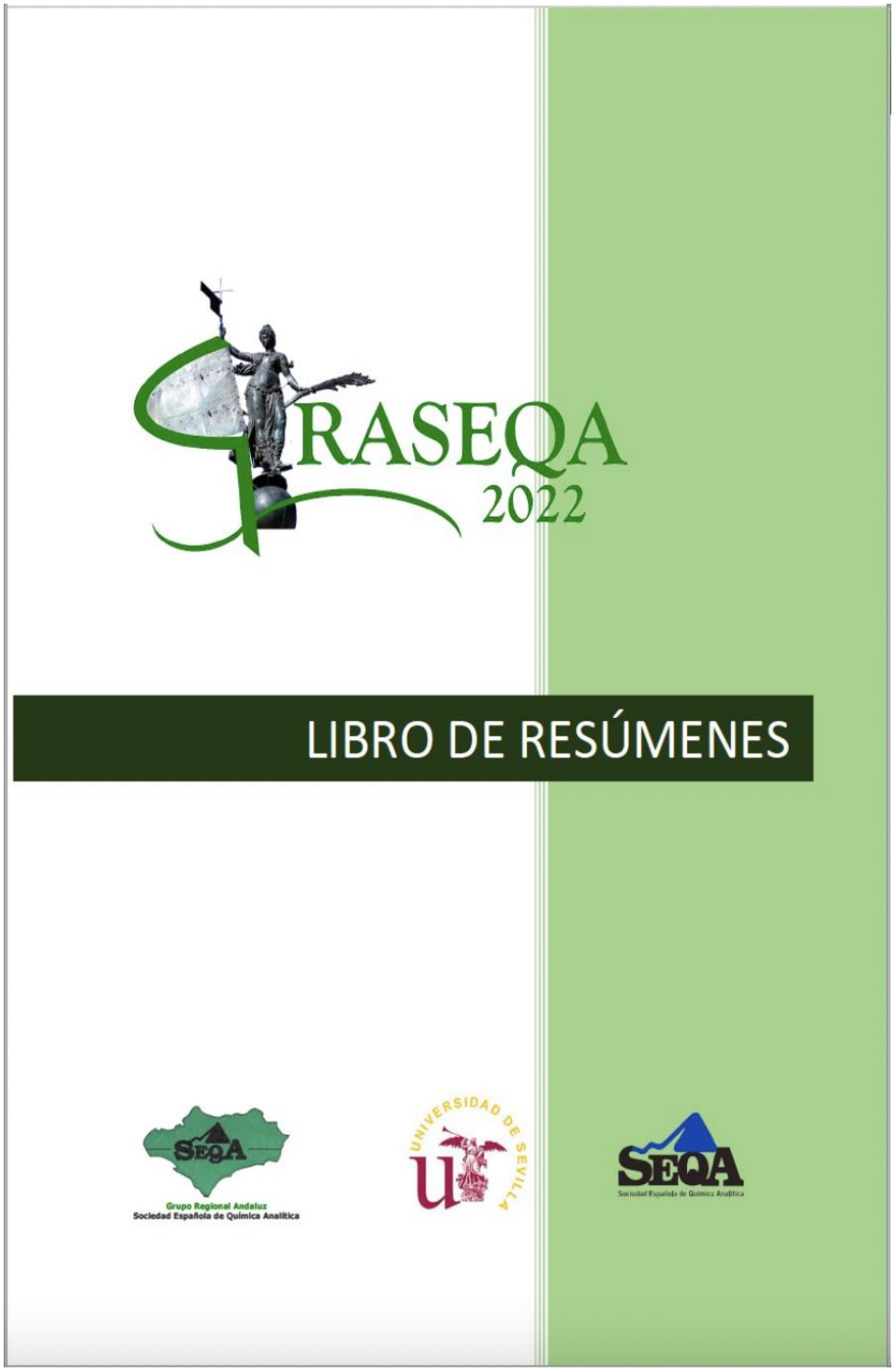
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P-073

DE UNA HORA A UN MINUTO: DETECCIÓN RÁPIDA DE BISPHENOLES EN PAPEL TÉRMICO MEDIANTE EL USO DE ESPECTROMETRÍA DE MASAS AMBIENTAL CON SUPRAS CONTENIDOS EN CAPILARES DE VIDRIO.

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En este trabajo se ha estudiado la compatibilidad de disolventes supramoleculares (SUPRAS) con el empleo de capilares de vidrio o sondas para la microextracción de compuestos y su posterior análisis mediante espectrometría de masas ambiental (*ambient mass spectrometry*, AMS) basada en ASAP (*atmospheric solids analysis probe*).

AMS consiste en la introducción directa de la muestra en el analizador. Existen diversas variantes, entre ellas la técnica ASAP, que consiste en colocar la muestra en un capilar de vidrio que es introducido directamente en la fuente APCI, siendo los analitos desorbidos por la alta temperatura de la fuente e ionizados por la corona de descarga.

El número de estudios relacionados con estrategias de preparación de muestras acopladas a AMS está aumentando rápidamente con el objetivo de mejorar la reproducibilidad, selectividad y sensibilidad de estas técnicas. En este sentido, los SUPRAS ofrecen múltiples ventajas como extractantes eficientes y adaptables a formatos de microextracción. Los SUPRAS son líquidos nanoestructurados formados por el autoensamblaje de agregados anfifílicos, que poseen múltiples sitios de unión y microambientes de diferente polaridad, lo que los convierte en excelentes candidatos para formatos de microextracción.

En este trabajo, se propuso una etapa de tratamiento de muestra simple y rápida, que consistió en cargar la sonda de ASAP con un pequeño volumen de SUPRAS (1,1–2 µL) y ponerla en contacto con las muestras durante 10 s para llevar a cabo la extracción de los compuestos de interés antes de su análisis. Se evaluaron diferentes tipos de SUPRAS sintetizados con agua, distintos disolventes orgánicos (etanol o tetrahidrofurano) y distintos anfifilos (ácidos carboxílicos, alcoholes y dioles, de distintas longitudes de cadena: C_6-C_{10}). El método se aplicó al cribado de bisfenol A y análogos en papel térmico. Los resultados óptimos se lograron con SUPRAS sintetizados con 1-decanol en mezclas de etanol:agua. Los picos de señal de AMS (ancho: 0,2–0,5 min) se integraron y normalizaron fácilmente con estándares internos (RSD: 2–25 %). Por el contrario, el análisis directo de sólidos generó una señal de MS continua y contaminación cruzada en la fuente debido a la liberación de partículas sólidas. Se analizaron un total de 62 muestras (tickets de supermercados, tiendas, gasolineras, etc.), siendo el BPA y el BPS los bisfenoles más frecuentes (este último más que el primero). Estos resultados ponen de manifiesto la progresiva sustitución industrial del BPA por el BPS debido a su regulación en papel térmico a partir del año 2020. El uso de otras alternativas como TGSA, Pergafast 201, D-8, etc., es aún es limitado.

Agradecimientos: A. Ballesteros-Gómez agradece la financiación a través de su contrato Ramón y Cajal (RYC-2015-18482) y M.J. Dueñas Mas por su beca predoctoral FPI (PRE2018-083336), ambas procedentes del Ministerio de Ciencia, Innovación y Universidades (Proyecto CTQ2017-83823R).


BOOK OF
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COMPARATIVE CHEMICAL PROFILING OF UNDEREXPLOITED *CITRUS SINENSIS* L. HERBAL DUST EXTRACTS OBTAINED BY SUBCRITICAL WATER AND PRESSURIZED ETHANOL EXTRACTIONS

***Krivošija S.*[1], *Ballesteros-Gómez A.*[2], *Dueñas-Mas M.J.*[2], *Tomić M.*[3], *Nastić N.*[1], *Sulejmanović M.*[1], *Vidović S.*[1]**

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Abstract

Extractions processess such as subcritical water extraction (SWE) or pressurized liquid extraction (PLE), that uses a liquid solvent under pressurized process conditions, enjoys a great deal of scientific interest. Among this group SWE is considered as the most promising. Safety, low price and green character of water, good yields of target compounds and reduced energy consumption, make this technique attractive for potential industrial applications. On the other hand, with PLE, it is also possible to use a mixture of water/ethanol and ethanol as solvents, because they are GRAS (generally recognized as safe) solvents. Therefore, the aim of this study was to compare SWE with pressurized ethanol extraction (PEE), to optimize the temperature as the most influential process parameter, and at the same time propose new streams for the valorization of waste from the filter tea industry - orange peel dust (OPD). OPD is the material left after the industrial processing of orange peel, containing particles lower than the pores of filter paper (<0.315 mm), and therefore cannot be used further in the final herbal filter tea production. But, it still contains a wide range of high value compounds that can be utilized. In order to determine the possibility of complete extraction of OPD, a series of experiments were performed, where the temperature was varied (120-220°C), while the pressure and time were constant. After that, the obtained extracts were analyzed by LC-MS/MS. The comparison was made on the basis of total phenolic content (TPC), as well as chemical characterization of the obtained extracts. TPC in both techniques (SWE and PEE) increased with increasing temperature and the maximum value was 35.67 [mg GAE/g dry weight] and 70.56 [mg GAE/g dry weight], respectively. The most abundant compounds in the obtained extracts were hesperidin and naringin, where the highest concentration was reached at SWE (temperature 160 °C) and was 662.82 [mg/L] for hesperidin, and 59.99 [mg/L] for naringin. Results described in this work show that SWE and PEE can significantly enhance extraction of valuable compounds from plant material, thus proving to be a value addition processes and potentially efficient techniques to be used at industrial level.

Keywords: Orange peel, herbal dust, subcritical water extraction, pressurized ethanol extraction, polyphenols, LC-MS/MS analysis.

Acknowledgements: This work has been supported by COST Action GREENERING, CA18224, funded by COST (European Cooperation in Science and Technology).

8.

Divulgación científica

Se han realizado diferentes actividades de divulgación científica, que incluyen la participación en el Paseo por la Ciencia (dos ediciones) y en la Noche Europea de los Investigadores, organizados por la Universidad de Córdoba, la divulgación mediante artículos científicos en colaboración con la GRASEQA y con la Unidad de Cultura Científica e Innovación de la Universidad de Córdoba, y divulgación mediante la asistencia a un colegio durante unas jornadas solidarias.

1. Participación en el Paseo por la Ciencia, organizada por la Universidad de Córdoba el día 6 de abril de 2019.

2. Artículo de divulgación publicado en el boletín de la GRASEQA. Dueñas-Mas, M.J., Ballesteros-Gómez, A., Rubio, S. 2019. Microextracción con disolventes supramoleculares de retardantes de llama organofosforados en polvo procedente de casas y centros educativos en España. Boletín GRASEQA (ISSN: 2254-1241) 23, 3-9.

3. Divulgación sobre la determinación de bisfenoles en papel térmico por la Unidad de Cultura Científica e Innovación de la Unidad de Córdoba el 5 de abril de 2022.

4. Participación en la Noche Europea de los Investigadores, organizada por la Universidad de Córdoba, el día 30 de septiembre de 2022.

5. Divulgación de la actividad del grupo Química Analítica Supramolecular en el colegio Almedina en colaboración con la asociación Autismo Córdoba. Jornadas solidarias de recaudación de fondos para la asociación autismo de Córdoba. 19 de diciembre de 2022.

6. Participación en el Paseo por la Ciencia, organizada por la Universidad de Córdoba el día 15 de abril de 2023.

D. Casimiro Jesús Barbado López, con DNI 8784222Q, secretario de la Asociación Profesorado de Córdoba por la Cultura Científica (APCCC), con sede social en Córdoba, C/ Doña Berenguela nº 2 e inscrita en el registro de asociaciones de Andalucía con el número 14/1/06230

CERTIFICO

Que María Jesús Dueñas Mas con DNI 80166518H, del Instituto Universitario de Nanoquímica de la Universidad de Córdoba, ha participado en el **Paseo por la Ciencia**, una actividad de 10 horas de duración, organizada por esta asociación, el día 6 de abril de 2019.

En Córdoba, a 14 de abril de 2019

FDO. Casimiro Jesús Barbado

Vº Bº
LA PRESIDENTA

VºBº: Francisco J Romero Salguero
Director del Instituto Universitario de Investigación en Química Fina y Nanoquímica

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Microextracción con disolventes supramoleculares de retardantes de llama organofosforados en polvo procedente de casas y centros educativos en España

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1. Introducción

Los retardantes de llama de organofosforados con sustituyentes arilo (aril-OPFRs) son retardantes de llama o plastificantes (entre otras funciones) que pueden encontrarse en una amplia variedad de productos y materiales, desde muebles y textiles, a coches y equipos electrónicos. Existe una creciente preocupación sobre la exposición humana a estos contaminantes debido a su ubicuidad en el ambiente, ya que al ser aditivos (no enlazados químicamente) pueden ser liberados fácilmente desde el producto, y su potencial toxicidad.

El polvo se ha convertido en una matriz relevante para la evaluación de la exposición a contaminantes orgánicos, especialmente aquellos procedentes de materiales y productos en ambientes interiores (edificios) [1]. La presencia de OPFRs en polvo ha sido detectada en numerosos estudios con niveles de concentración del orden de ng·g-1 a mg·g-1 y con frecuencias de detección elevadas [2,3]. Los OPFRs son clasificados en tres grupos, según su composición: alquil-OPFRs, aril-OPFRs y OPFRs clorados [1]. En este estudio, se investigó la presencia de 6 aril-OPFRs, dos de ellos muy conocidos (trifenil fosfato, TPHP y 2-etilhexil difenil fosfato, EHDPP), dos emergentes (cresil difenil fosfato, CDP e isodecil difenil fosfato, IDPP) y dos oligoméricos [bisfenol A bis(difenil fosfato), BDP y resorcinol bis(difenil fosfato, RDP] en polvo de casas y centros educativos de España.

Mientras que EHDPP y TPHP han sido ampliamente estudiados, existen pocos datos sobre los aril-OPFRs emergentes como IDPP y CDP y sobre los oligoméricos, como BDP y RDP [4-6]. La presencia de aril-OPFRs emergentes y oligoméricos en centros educativos no ha sido apenas estudiada hasta la fecha, y además, aún no han sido determinados en polvo procedente de casas de España.

En este estudio, se analizaron aril-OPFRs en muestras de polvo usando disolventes supramoleculares (SUPRAS). Los SUPRAS son líquidos nanoestructurados producidos espontáneamente mediante autoensamblaje y coacervación de dispersiones coloidales de agregados anfifílicos debido a la presencia de un agente coacervante (cambio de pH o temperatura, deficiencia de solvente para el anfifilo y/o adición de sales) [7]. Son potentes extractantes que ofrecen una gran variedad de interacciones (iónicas, aniónicas, puentes de hidrógeno, fuerzas de dispersión, etc.), las

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DE UNA HORA A UN MINUTO: UNA NUEVA TÉCNICA DE ANÁLISIS SIMPLIFICA EL PROCESO PARA DETECTAR CONTAMINANTES

Escrito por UCC+i

El contaminante bisfenol A es un compuesto químico empleado principalmente en la fabricación de plásticos

Un nuevo trabajo de investigación consigue, mediante el empleo de disolventes ecológicos y espectrometría de masas ambiental, abaratar el proceso y reducir el tiempo necesario para detectar bisfenoles, compuestos tóxicos para el organismo según diversos estudios y prohibido en algunos productos de la UE


LA NOCHE EUROPEA
DE L@S INVESTIGADOR@S
MUJERES Y HOMBRES QUE HACEN CIENCIA PARA TI
Diploma
María Jesús Dueñas Mas
Ha participado en las Jornadas de La Noche Europea de los
Investigadores el 30 de septiembre de 2022 en calidad de Ponente
Teresa Cruz Sánchez. Directora de la Fundación Descubre
Organizan
Financian
Junta de Andalucía
Funded by the European Union

UNIVERSIDAD D CÓRDOBA

VICERRECTORADO POLÍTICA CIENTÍFICA

María José Polo Gómez, vicerrectora de Política Científica de la Universidad de Córdoba,

INFORMA:

Que Dña. **María Jesús Dueñas Mas** ha participado como ponente en unas jornadas de divulgación científica de 4 horas de duración celebradas el pasado 17 de diciembre. El evento, de carácter benéfico y desarrollado con el objetivo de ayudar económicamente a la asociación Autismo Córdoba, ha contado con la colaboración de la Unidad de Cultura Científica de la Universidad de Córdoba

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Lo que comunico para su conocimiento y efectos administrativos.

Córdoba, 15 de febrero de enero de 2023

María José Polo Gómez
Vicerrectora de Política Científica

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