



Editorial Molecularly Imprinted Polymers: Selective Extraction Materials for Sample Preparation

Antonio Martín-Esteban 回

Department of Environment and Agronomy, National Institute for Agricultural and Food Research and Technology, Spanish National Research Council (INIA, CSIC), 28040 Madrid, Spain; amartin@inia.csic.es

1. Introduction

Highly developed analytical instrumentation (i.e., chromatographic techniques coupled to mass spectrometry) is now available in most analytical laboratories; thus, it is possible to determine any kind of organic compound. However, the direct analysis of crude sample extracts negatively affects the quality of the obtained results in terms of both precision and accuracy, and potentially damages the detection equipment. Therefore, an adequate sample preparation should be performed before final determination in order to reduce the matrix effect during the subsequent measurement step. Moreover, sample preparation allows an increase in the concentration (trace enrichment) of target analytes, which in turn allows researchers to reach the low-detection limits necessary to meet the current stringent regulations established by national and international authorities. Other sample-preparation objectives-such as reducing both the sample size and the amount of organic solvents and glassware to be used, facilitating automatization, and increasing sample throughput-have been established during the last decades. The pursuit of these objectives has led to the development of improved analytical methods in terms of accuracy and precision, as well as a decrease in hazardous wastes in accordance with the Ten Principles of Green Sample Preparation [1]. Accordingly, the development of new miniaturised analytical techniques/devices and new adsorbent materials have been research areas of great activity during last years. Several microextraction techniques, such as micro solidphase extraction (μ -SPE), solid-phase microextraction (SPME), stir bar sorptive extraction (SBSE), and liquid-phase microextraction (LPME), have been developed in order to fulfil the objectives mentioned above. Alongside these developments, a great variety of new sorbents, such as restricted access materials, carbon-based sorbents (carbon nanotubes and graphene), metal organic frameworks, coated magnetic nanoparticles, among others, have shown excellent adsorption capacity for target analytes from a complex matrix [2,3].

Irrespective of the sorbent to be used, the extraction process is mainly governed by non-selective interactions between analytes and functional groups present on the sorbent. Such lack of selectivity makes necessary an extensive optimization of the typical steps involved, but, even after careful optimization, some matrix components are co-eluted with target analytes. In order to improve the selectivity of the extraction process, molecularly imprinted polymers appear to be a good choice.

Molecularly imprinted polymers (MIPs) are tailor-made materials able to selectively bind a target analyte in preference to other closely related compounds and under certain experimental conditions [4,5]. MIPs are obtained by polymerizing functional and crosslinking monomers around a template molecule, a process that leads to a highly cross-linked, three-dimensional network polymer. The monomers are chosen by considering their ability to interact with the functional groups of the template molecule. Once polymerization has taken place, the template molecule is extracted, and binding sites with shape, size, and functionalities complementary to the target analyte are established. Thus, the resulting imprinted polymers are able to rebind a target analyte, leading to extraction methods with improved selectivity [6]. Moreover, by clever (and rather simple) modifications of



Citation: Martín-Esteban, A. Molecularly Imprinted Polymers: Selective Extraction Materials for Sample Preparation. *Separations* **2022**, *9*, 133. https://doi.org/10.3390/ separations9050133

Received: 12 May 2022 Accepted: 21 May 2022 Published: 23 May 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). polymerization procedures, MIPs can be incorporated into current sample-preparation micro-extraction techniques without affecting their inherent selectivity and stability [7,8].

Accordingly, the present Special Issue collects several papers dealing with recent developments on the incorporation of MIPs into sample-preparation methods.

2. Summary of Published Articles

MIPs have been widely used as sorbents in conventional solid-phase extraction, socalled molecularly imprinted solid-phase extraction (MISPE), allowing the performance of a customised sample treatment step prior to final determination, and today this is by far the most developed strategy for the use of MIPs in sample preparation. This statement is nicely demonstrated in the paper by Bosman el al. [9], published in this Special Issue. Bosman et al. examine the development and application of MIPs for the selective extraction of chlordecone in bovine serum. The widespread use of chlordecone (CLD), an organochlorine pesticide, to protect banana crops in the French West Indies, a practise that lasted until the 1990s, led to significant pollution of water and soil and, subsequently, of bovine intended for human consumption. In order to allow for pre-slaughter controls, a new MIP was synthesised and fully optimised to be used in solid-phase extraction associated with the final determination of chlordecone by LC/MS-MS. The proposed method provides quantitative recoveries leading to cleaner extracts than those achieved by a conventional C_{18} sorbent. The great selectivity provided by the MIP cartridge allows the simplification of the serum pre-treatment step (a single acetonitrile-precipitation step), leading to a limit of quantification of the global analytical procedure of 4.4 ng L^{-1} , which is 5 to 180 times lower than those provided by conventional methods.

The preparation of MIPs requires a large amount of the template, which sometimes is difficult to find, expensive, unstable, or it represents a hazard to health or safety. Moreover, the complete removal of the template from the imprinted polymer is not easily achieved; thus, template residues slowly leach out and contaminate the samples in the solid-phase extraction process. To overcome these drawbacks, the "mimic template" or "dummy template" approach has been proposed, although a large amount of the dummy template is still required. As an alternative, the synthesis of nanoMIPs by solid-phase synthesis has been proposed [10,11]. In this approach, since the template molecules are covalently grafted onto glass beads, no residual template molecules are present in the resulting nanoMIPs, avoiding the bleeding effect entirely. Furthermore, because functionalized glass beads require a small amount of the template and can be reused many times, this approach allows the use of expensive templates.

NanoMIPs have proven to be very versatile, but to date only limited attention has been paid to their use in solid-phase extraction; thus, the paper by Chiarello et al. [12] of the present Special Issue focuses on the ability of nanoMIPs to extract fluoroquinolone antibiotics from human urine by MISPE. Several nanoMIPs were prepared in water with polymerization mixtures of different compositions, and the polymer with the highest affinity towards ciprofloxacin was then grafted onto a solid support and used to set up a solid-phase extraction–HPLC method with fluorescence detection. It was observed that the nanoMIPs were suitable for direct extraction of the target antibiotics from the urine samples at the μ g mL⁻¹ concentration level. Without preliminary treatments (just a dilution with a buffer), recoveries of up to 85%, with precision in the range of 3% to 4.5% and without interference from the matrix, were achieved. These results demonstrate the feasibility of the use of nanoMIPs in the development of MISPE procedures and open new areas of research in the molecular imprinting field.

As mentioned above, MIPs can be incorporated into other sample-preparation microextraction techniques. For example, the incorporation of MIPs to Dispersive (Micro)Solid Phase Extraction (D- μ -SPE) has received special attention in recent years, and it is reflected in this Special Issue in the comprehensive review by Thilini Madurangika Jayasinghe and Moreda-Piñeiro [13] and in the article by Mpayipheli et al. [14] devoted to the development of a Vortex-Assisted Dispersive Molecularly Imprinted Polymer-Based Solid Phase Extraction method for the determination of acetaminophen from water samples.

Molecularly Imprinted-D- μ -SPE consists of dispersing the imprinted polymer particles (a few milligrams) into the sample or the sample extract by shaking (oscillators and vortex) or sonication or by magnetic stirring when magnetic sorbents are used. Dispersion of the sorbent in the sample maximizes disaggregation of sorbent particles, thus increasing the surface area available. This approach enhances target analytes adsorption on the sorbent and represents a rather simple but effective alternative to traditional SPE. Furthermore, the great variety of MIPs for D- μ -SPE (magnetic and non-magnetic composites) has allowed the development of several applications based on the use of quite different MIP-based sorbents for the trace enrichment and clean-up of target analytes in environmental, food, and bio-samples.

3. Conclusions

The papers included in this Special Issue demonstrate that the use of MIPs provides a simple way for the development of simple, robust, flexible, and highly selective (micro)extraction methods with improved analytical characteristics. Moreover, it is possible to adapt MIP preparation to be incorporated into (micro)extraction and solventless techniques.

In spite of the relevant advances in the molecular imprinting field achieved during last two decades, there is still room for improvement in terms of MIP performance and in widening the fields of application. In this regard, the refinement of the use of MIPs in well-established sample-preparation techniques as well as the development of formats and devices with some degree of automatization will bring new selective, simple analytical methods in the near future.

Funding: This research received no external funding.

Acknowledgments: A.M.-E. thanks all the authors for their excellent contributions. The efforts of the reviewers are acknowledged as contributing greatly to the quality of this Special Issue.

Conflicts of Interest: The authors declare no conflict of interest.

References

- López-Lorente, Á.I.; Pena-Pereira, F.; Pedersen-Bjergaard, S.; Zuin, V.G.; Ozkan, S.A.; Psillakis, E. The ten principles of green sample preparation. *TrAC—Trends Anal. Chem.* 2022, 148, 116530. [CrossRef]
- Chen, Y.; Xia, L.; Liang, R.; Lu, Z.; Li, L.; Huo, B.; Li, G.; Hu, Y. Advanced materials for sample preparation in recent decade. *TrAC—Trends Anal. Chem.* 2019, 120, 115652. [CrossRef]
- Maciel, E.V.S.; de Toffoli, A.L.; Neto, E.S.; Nazario, C.E.D.; Lanças, F.M. New materials in sample preparation: Recent advances and future trends. *TrAC—Trends Anal. Chem.* 2019, 119, 115633. [CrossRef]
- Wulff, G.; Sarhan, A. Über die Anwendung von enzymanalog gebauten Polymeren zur Racemattrennung. Angew. Chem. 1972, 84, 364. [CrossRef]
- 5. Arshady, R.; Mosbach, K. Synthesis of substrate-selective polymers by host-guest polymerization. *Makromol. Chem.* **1981**, *182*, 687–692. [CrossRef]
- 6. Martín-Esteban, A. Molecularly-imprinted polymers as a versatile, highly selective tool in sample preparation. *TrAC—Trends Anal. Chem.* **2013**, 45, 169–181. [CrossRef]
- 7. Turiel, E.; Martín-Esteban, A. Molecularly imprinted polymers-based microextraction techniques. *TrAC—Trends Anal. Chem.* 2019, 118, 574–586. [CrossRef]
- Bouvarel, T.; Delaunay, N.; Pichon, V. Molecularly imprinted polymers in miniaturized extraction and separation devices. *J. Sep. Sci.* 2021, 44, 1727–1751. [CrossRef] [PubMed]
- 9. Bosman, P.; Combès, A.; Lambert, M.; Lavison-Bompard, G.; Pichon, V. Development and Application of Molecularly Imprinted Polymers for the Selective Extraction of Chlordecone from Bovine Serum. *Separations* **2021**, *8*, 237. [CrossRef]
- Poma, A.; Guerreiro, A.; Whitcombe, M.J.; Piletska, E.V.; Turner, A.P.F.; Piletsky, S.A. Solid-Phase Synthesis of Molecularly Imprinted Polymer Nanoparticles with a Reusable Template–"Plastic Antibodies". *Adv. Funct. Mater.* 2013, 23, 2821–2827. [CrossRef] [PubMed]
- 11. Ambrosini, S.; Beyazit, S.; Haupt, K.; Tse Sum Bui, B. Solid-phase synthesis of molecularly imprinted nanoparticles for protein recognition. *Chem. Commun.* **2013**, *49*, 6746–6748. [CrossRef] [PubMed]
- 12. Chiarello, M.; Anfossi, L.; Cavalera, S.; Di Nardo, F.; Serra, T.; Baggiani, C. NanoMIP-Based Solid Phase Extraction of Fluoroquinolones from Human Urine: A Proof-of-Concept Study. *Separations* **2021**, *8*, 226. [CrossRef]

- 13. Jayasinghe, G.D.T.M.; Moreda-Piñeiro, A. Molecularly Imprinted Polymers for Dispersive (Micro)Solid Phase Extraction: A Review. *Separations* **2021**, *8*, 99. [CrossRef]
- 14. Mpayipheli, N.; Mpupa, A.; Nomngongo, P.N. Vortex-Assisted Dispersive Molecularly Imprinted Polymer-Based Solid Phase Extraction of Acetaminophen from Water Samples Prior to HPLC-DAD Determination. *Separations* **2021**, *8*, 194. [CrossRef]