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Review

Theranostic advances and the role of molecular imprinting in disease management

Eylul Gulsen Yilmaz,[1,2] Beyza Nur Küçük,[1,2] Yusuf Aslan,[1,2] Özgecan Erdem,[1] Yeşeren Saylan,[3] Fatih Inci,[1,2] and Adil Denizli[3,*]

[1]UNAM—National Nanotechnology Research Center, Bilkent University, Ankara 06800, Turkey
[2]Institute of Materials Science and Nanotechnology, Bilkent University, Ankara, Turkey
[3]Department of Chemistry, Hacettepe University, Ankara, Turkey
*Correspondence: denizli@hacettepe.edu.tr
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SUMMARY

Molecular imprinting has become an effective technology in the realm of diagnosing diseases, providing unparalleled specificity and sensitivity. This method is a promising trend in current medical research. This review examines the utilization of molecularly imprinted polymers (MIPs) in theranostic that integrates diagnostic functionalities for personalized medicine. The present work briefly discusses the fundamental concepts of molecular imprinting and how it has evolved into a versatile platform. Subsequently, the utilization of MIPs in the advancement of biosensors is focused, specifically emphasizing their contribution to the detection and diagnosis of diseases. The therapeutic potential of MIPs, focusing on targeted drug delivery and controlled release systems and the integration of MIPs into theranostic platforms is explored through case studies, showcasing the technology's ability to simultaneously diagnose and treat diseases. Finally, we address the current challenges facing MIPs and discuss future perspectives, emphasizing the potential of this technology to revolutionize the next generation.

INTRODUCTION

The combination of bioimaging and therapy, known as "theranostics," has been studied over the last 70 years[1] and has seen rapid progress over the past decade due to advancements in radiotheranostics,[2] photonics,[3] photodynamic therapy,[4] and nanoparticles (NPs).[5] These advancements in theranostics have brought larger public access to personalized medicine. Yet, one significant challenge remains to be solved: reliance on biological targeting agents, such as antibodies and peptides. These agents provide high target affinity, but they are physically and chemically unstable, which increases the cost and patient incompatibility in large production scales. Molecularly imprinted polymers (MIPs) are considered the chemical mimics of antibodies and address these drawbacks by using a nonhydrolyzable polymer backbone with a variety of functional monomers. The functional monomers mimic the side chains of 20 amino acids found in antibodies. Some of the example monomers are methacrylic acid (Glu and Asp), methacrylamide (Gln, Asn), and aminoethyl methacrylate (Lys).[6] Most importantly, MIPs demonstrate superior chemical and thermal stability, which is not achieved by most biological recognition elements, such as antibodies.[7] Furthermore, they can be synthesized with ease and can be reused multiple times.[8,9] Considering the resources and time required for synthesizing any type of biological recognition element, MIPs offer much greater cost-effectiveness and easier scalability.[10] They achieve these outstanding features while maintaining similar sensitivity and selectivity with biological recognition elements.[11,12] These advantages make them ideal for their use in robust and reusable platforms, which are highly suited for diagnostic and therapeutic applications. Furthermore, researchers have tailored MIPs that can demonstrate stimuli-responsive behavior. These MIPs release therapeutic agents in response to environmental change, such as pH.[13]

In the process of MIPs synthesis, these functional monomers are spatially imprinted around the target molecule by forming a template through either covalent or noncovalent interactions. The template and functional monomers are copolymerized with a cross-linker in a compatible solvent. Subsequently, the template is removed, and complementary cavities are formed. These cavities align with the spatial positions of the functional groups found in the template and complement the size, shape, and positions of functional groups. The interactions between the template (guest) and the monomers (host) are primarily mediated by noncovalent interactions, such as hydrogen bonding, electrostatic forces, and van der Waals forces.[14] These guest-host interactions enable stable and efficient imprinting of the template, allowing specific recognition of target molecules. Traditionally the choice of functional monomers have been chosen by a trial-and-error approach using common functional monomers like methacrylic acid and vinyl pyridine. However, molecular dynamics simulations are now also employed as an additional tool for computational design and interaction modeling.[15] After synthesis, imprinted polymers are mainly characterized and the polymer-template binding strength is quantified using nuclear magnetic resonance (NMR),[16] surface plasmon resonance

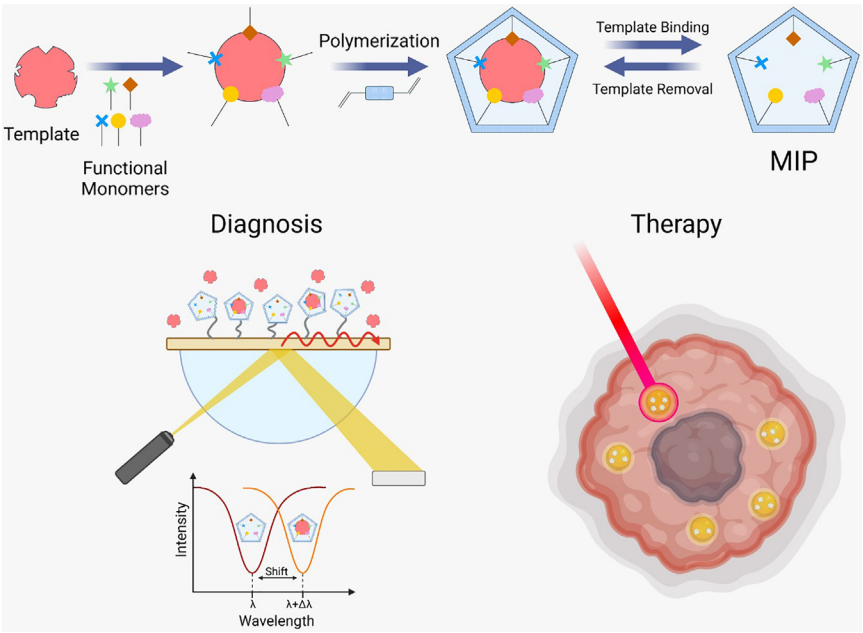

Figure 1. Schematic illustration of MIP synthesis steps and their applications in theranostics

Below the synthesis process, examples of diagnostic and therapeutic techniques, including SPR and laser metal nanoparticle irradiation, are depicted. Created with BioRender.com (accessed on 2 November 2024).

(SPR),[17] and calorimetric titrations.[18] Through these synthesis and characterization steps many analytes have been molecular imprinted. Some of the examples include small molecules, metal ions,[19] pesticides,[20] toxins, radioactive compounds,[21] amino acids, proteins, drugs,[22] bacteria,[23] and viruses.[24] Recently, the specific recognition of the polar head groups of phospholipids has been demonstrated, highlighting the applicability of molecular imprinting in targeting exosomes and monitoring cell apoptosis.[25,26] These molecular imprints have been employed in a variety of applications, including solid phase extraction,[27] chromatographic separations,[28] immunoassays,[29] and biosensors. The discovery of aqueous-compatible MIP NPs has greatly expanded their potential in bioimaging and therapeutic applications.[30] Labeling these MIP NPs provided combined fluorescence imaging and selective capture of tumor cells[31] or tumor site drug delivery.[32] The preparation of these multifunctional platforms can be achieved through numerous polymerization methods. Some of the examples are precipitation,[33] high dilutions,[34] core-shell,[35] and surface-imprinted. Precipitation polymerization is a straightforward method for synthesizing MIP NPs ranging between 100 and 300 nm and is widely preferred in many studies. Following, high dilution method provides the synthesis of smaller MIP NPs (down to 14 nm)[36] by preventing the macrogel formation in highly solvated medium.[37] Emulsion polymerization occurs inside a two-phase system, such as oil/water and water/oil mediums. In this method, the template and monomers present inside surfactant micelles and an initiator in continues phase penetrates inside the micelle and initiates the polymerization process. With this method, uniform MIPs ranging between 10 and 100 nm are obtained, although their purification can be lengthy and incomplete.[38] Core-shell method utilizes noble metal NPs.[39] magnetic particles,[40] quantum dots (QDs)[41] and organic polymers[42] as core material and grafts the MIPs over the core particles using bottom-up fabrication. This method is especially useful for functionalizing the MIPs. Surface-imprinting aims to minimize the steric hindrance by grafting imprints on a support material, such as silica.[43] These preparation methods provide a versatile toolkit for developing MIPs tailored to theranostic applications. In this review, we will examine MIPs specifically designed for disease diagnosis and therapeutic applications, followed by a discussion of their combined theranostic roles (Figure 1).

This review initially provides the fundamentals of molecular imprinting by explaining common imprinting polymerization methods to equip the reader with the necessary literature for grasping the working principles of molecular printing. Then, the usage of MIPs in disease diagnostics on biosensors and therapy development is individually and comprehensively reviewed. Types of biosensors were divided into sub-categories depending on their physical transducing mechanism: electrochemical, optical, and piezoelectric. Then, a special part focused on the impact of MIPs in several critical disease groups: cancer, infectious, and chronic diseases. The review also underlines the advancements in therapeutic applications, especially focusing on drug delivery platforms and specialized cancer treatments. Building the foundations of MIP applications on diagnosis and therapy, we emerged into theranostic applications where two separate foundations merge into one. Lastly, we address the current challenges hindering the clinical translation of MIPs and provide insights into future directions. Our review distinguishes itself from the current literature by providing a comprehensive view of diagnostic, therapy, and theranostics. The current literature is flourishing with the advancements of molecular and ionic imprinting chemical assays,[44,45] the discovery of new techniques on molecularly imprinted solid phase extraction,[46] cancer-focusing diagnostic strategies,[47] advanced drug delivery approaches,[48] and the introduction of machine learning (ML) integration.[49] Specifically, our article provides a new scope to the literature by not only drawing attention to the recent advances of MIPs in diagnostics and therapy through extensive discussions but also highlighting their unification into theranostic applications.

MOLECULAR IMPRINTING FOR DISEASE DIAGNOSIS

Disease detection, bioassays, drug delivery, cancer therapy, toxin neutralization, therapeutics, and bioimaging are just a few

of the many areas that have found use for MIPs due to their versatility.[50–53] They have proven to be very useful in the detection and quantification of analytes in biological samples, including microbes, environmental contaminants, disease biomarkers, and toxins in saliva, blood, and urine.[54–56] Wearable devices utilizing MIPs-based biosensors have demonstrated significant potential for robust, long-term monitoring under challenging environments. In addition, artificial antibody-integrated biosensors utilizing point-of-care testing (POCT) with MIP technology have become an essential tool for offering patients individualized diagnostic information.

This review examines the implementation of molecular imprinting technology, with a primary emphasis on its application in biosensing. Nonetheless, a notable use in the field of illness surveillance is imaging. MIPs have demonstrated significant potential in improving imaging methodologies, especially in medical diagnostics. By developing highly selective binding sites that emulate natural antibodies, MIPs can serve as contrast agents in imaging techniques such as magnetic resonance imaging (MRI) and fluorescence imaging. This program facilitates enhanced targeting and viewing of specific biomarkers, therefore augmenting the precision of disease diagnosis and monitoring. The dual functionality of MIPs in sensing and imaging highlights their adaptability and significance in enhancing disease surveillance technologies.

Biosensor development using MIPs

In several areas, including as pharmaceuticals, environmental monitoring, food safety, therapeutics and clinical diagnostics, biosensors have become indispensable for the precise identification and quantification of target analytes.[57] These instruments find out what kind of analyte it is and how concentrated it is by converting molecular recognition elements into measurable signals.[58] Biological receptors, such as antibodies or enzymes, are the backbone of traditional biosensors; nevertheless, they aren't always reliable, can be expensive, and exhibit batch-to-batch variability.[59] The emergence of synthetic alternatives such MIPs that are engineered to connect with target molecules offers a potential solution. Stability, affordability, and convenience of production are the three main selling points of these custom-made chemical receptors.[60] Their use in *in vitro* and *in vivo* biosensing has been greatly improved by the introduction of biocompatible MIPs.[61] Medical diagnostics, therapeutic monitoring, food safety, and environmental management are some of the many applications that benefit greatly from MIPs-based biosensors due to their fast, on-site capabilities.[62] Their stability and specificity make them useful in many different contexts, and their employment solves numerous problems.[63]

To guarantee good diagnostic potential, numerous critical criteria must be considered in the design of biosensors, particularly for *in vitro* diagnostics (IVD).[64] The compact setup requires minimum instrumentation, low sample quantities, and minimal sample processing. It also has a good signal-to-noise ratio and is sensitive enough to detect low-abundance biomarkers, which are critical for early-stage diagnosis.[65] The ability of biosensors to reliably detect changes in a wide range of environmental factors depends on their resistance to interference from complicated biological matrices.[66] One factor that has contributed to MIPs' commercial viability is their incorporation into biosensor systems as artificial biorecognition elements. The development of MIPs-based biosensors has been further expedited by recent advances in MIPs synthesis, assisted by computational design, and the shrinking of transducer platforms. Improvements in stability, robustness, and scalability have allowed these biosensors to be mass-produced.[64] Based on their success with electrochemical biosensors, MIPs have branched out to include optical (e.g., SPR, piezoelectric (e.g., quartz crystal microbalance, QCM), and thermal sensing technologies[67] (Table 1). In addition, state-of-the-art technologies are incorporating MIPs into lateral flow lab-on-chip assays and microfluidic analytical systems, which increases their potential for commercial and point-of-care applications.

However, many obstacles, such as nonspecific binding, difficulty in template extraction, and an absence of defined methods, have slowed the commercialization of MIPs, notwithstanding their potential.[80] Nonetheless, MIPs have shown increasing market potential, since multiple companies have commercialized them.[81] One of the pioneers in commercializing MIPs was a Swedish company called ''MIP Technologies,'' which Biotage AB eventually bought.[82] The Israeli company Semorex Ltd. is working on MIPs for diagnostic and therapeutic purposes, with an emphasis on fungal infections. The French company Polyintell SAS created the ''AFFINIMIP'' range of products, whereas the Spanish firm NanoMyp is an expert in micro- and NPs used in MIPs. Prof. Sergey Piletsky established MIP Diagnostics Ltd. to create nanoMIP products for use in point-of-care diagnostics. The commercial success of MIPs is further demonstrated by Sigma Aldrich's SupelMIP columns, which are used for solid-phase extraction. Even if there are still issues with standardization and scalability, these examples show that MIPs have great potential for commercial applications.

Recent improvements in MIP commercialization have been supported by patents, underscoring the continuous progress in the sector. MIP Technologies AB has notably submitted patents for the production of affinity MIPs that are included in their biosensor systems.[83] Semorex Inc. has submitted patents for molecular imprinting techniques and diagnostic kits aimed at detecting fungal infections by measuring ergosterol levels.[84] Additionally, patents illustrate the application of MIPs for the binding of bile acids, including deoxycholic acid (DCA), which may be pivotal in the diagnosis and treatment of ailments such as gallstones, colorectal cancer, and inflammation. These improvements highlight the expanding market potential and future applications of MIPs across several commercial sectors.

Electrochemical biosensors

Electrochemical biosensors have significantly influenced the global market owing to their exceptional sensitivity.[67] Conventional biosensors depend on electro-active molecules affixed to electrodes; however, the instability of bioreceptors frequently results in interference and nonspecific adsorption in actual samples.[85] Attempts to enhance biosensor interfaces using functional materials have not entirely addressed these problems. The irreversible nature of receptor-analyte interactions diminishes sensitivity and stability.[86,87] Consequently, traditional

Table 1. MIP based biosensors with different transducing mechanisms

Transducing Mechanism	Type of Signal Detected	Biomarker/Analyte	Detection Range	LOD	Reference
Electrochemistry	Cyclic Voltammetry	nCOVNP	2.22–111 fM	15 fM	Raziq et al.[68]
		CA 15-3	0.10–100 U/mL	0.10 U/mL	Ribeiro et al.[69]
		p-Tau-441	2.18 p.m.−2.18 nM	0.02 p.m.	Ben Hassine et al.[70]
	Pulsed Amperometry	*Listeria monocytogenes*	300–6700 CFU/mL	70 CFU/mL	Liustrovaite et al.[71]
	Differential Pulse Voltammetry	Protein E2	0.01–50 ng/mL	0.46 pg/mL	Antipchik et al.[72]
	Square Wave Voltammetry	Insulin	0.050–1.40 p.m.	33 fM	Wardani et al.[73]
Optical Detection	Fluorescence	THZ	4–120 nmol/L	0.43 nmol/L	Ensafi et al.[74]
	Wavelength Interrogation Technique	IPA vapor	–	0.63 nm/%IPA	Pathak et al.[75]
	SERS	CEA	0.1 pg/mL−10 μg/mL	0.064 pg/mL	Lin et al.[76]
Piezoelectricity	Frequency	*Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*	–	–	Tokonami et al.[77]
		Bilirubin	1–50 μg/mL	0.45 μg/mL	Çiçek et al.[78]
		H5N1	–	1 HA titer unit	Wangchareansak et al.[79]

electrochemical biosensors fail to satisfy actual application requirements. MIPs-based electrochemical biosensors provide improved sensitivity and stability, addressing numerous constraints.[88]

An electrochemical sensing-based portable diagnostic device for the detection of SARS-CoV-2 nucleoprotein (ncovNP) was developed using MIPs during the COVID-19 pandemic.[68] The creation of an electrochemical biosensor based on MIPs for the detection of SARS-CoV-2 nucleoprotein (ncovNP) was first demonstrated by this platform. The biosensor uses a disposable thin film electrode biosensor device with MIP-endowed ncovNP selectivity and a portable potentiostat. The biosensor responded linearly to ncovNP in the lysis buffer up to 111 fM with a detection and quantification limit of 15 and 50 fM, respectively.[68] The biosensor detected ncovNP in COVID-19-positive nasopharyngeal swabs. The proposed technique opened a new path for quick COVID-19 diagnostics. In another study MIPs-based electrochemical biosensor was used to detect *Listeria monocytogenes*. The study designed an electrochemical biosensor using platinum (Pt) and screen-printed carbon electrodes (SPCE) modified by MIP.[71] The non-imprinted polypyrrole (NIP-Ppy) and *Listeria monocytogenes*-imprinted polypyrrole (MIP-Ppy) layers were electrochemically deposited over SPCE and Pt electrodes using a potential pulse sequence (Figure 2A). MIP-Ppy- and NIP-Ppy-modified electrodes were tested by pulsed amperometric detection. This research suggests that trypsin can be used to remove germs to create the best MIP-Ppy/SPCE biosensor. Limit of detection (LOD) and limit of quantification (LOQ) of MIP-Ppy/SPCE were 70 and 210 CFU/mL, respectively, with a linear range of 300–6700 CFU/mL.[71]

Optical biosensors

A range of optical biosensors is employed for the precise measurement of light and molecular interactions. These encompass fluorescence, SPR, and surface-enhanced Raman scattering (SERS).[89] MIPs-based optical biosensors incorporate MIPs as the recognition unit to specifically engage and bind with the target, together with a transducer component to signal the binding event.[90] Their emphasis was on quantifying the alterations in the optical responses of the transducer due to creating a complex between the target and MIPs, thereby offering an efficient, quick, and economical sensing technique for sensitive detection based on the diverse optical signals detected.[91]

In order to detect thioridazine hydrochloride (THZ), a neuroleptic medicine used to treat schizophrenia and other psychiatric illnesses, Ensafi et al. developed an optical biosensor with particular binding sites.[74] ZnO QDs covered with MIPs formed the biosensor. Reverse microemulsion was used to fix the MIPs layer on ZnO-QDs after precipitation from $Zn(CH_3COO)_2$ and NaOH. As THZ concentration increased, QDs-MIPs fluorescence intensity decreased. In ideal circumstances, THZ can be detected with a low detection limit of 0.43 nmol L^{-1} and a linear dynamic range of 4–120 nmol L^{-1}. Many volatile organic chemicals (VOCs) in human exhaled breath are being used as biomarkers to identify diseases, including diabetes, thanks to recent developments. Type 1 and type 2 diabetics' exhaled breath contains isopropanol (IPA). An experimental attempt to developing a highly selective and sensitive IPA vapor biosensor system is developed by Pathak et al.[75] The biosensor is a tiny, portable glass slide coated with MIP with IPA-compatible binding sites (Figure 2B). This biosensor uses wavelength

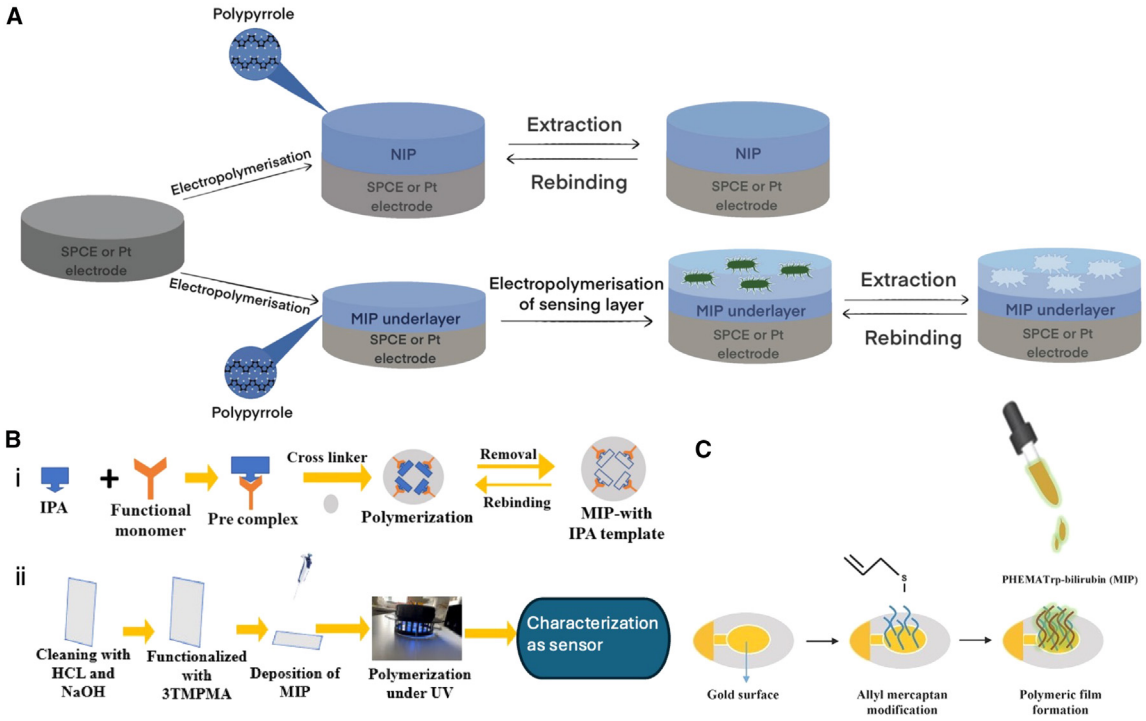

Figure 2. Electrode functionalization and biosensor fabrication strategies for selective analyte detection

(A) Schematic illustration for electrode modification

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(B) Creating a highly selective and sensitive IPA vapor biosensor system. (1) Schematic representation of the synthesis process. (2) Diagram of biosensor production encompassing surface functionalization and polymerization processes. Reproduced with permission from.[75]

(C) A non-enzymatic bilirubin detection biosensor using a QCM biosensor coated with a bilirubin-imprinted PHEMATrp polymeric film, designed for the potential diagnosis of hyperbilirubinemia. Reproduced with permission from.[78]

interrogation. A device is tested for IPA vapor detection at 50%–100% concentrations. The biosensor has strong selectivity among a similar class of VOCs with maximum sensitivities of 0.37, 0.30, and 0.62 nm/%IPA for 30, 60, and 90 min, respectively. It also has an exceptional sensitivity of 0.63 nm/%IPA for 120 min. The biosensor's small size, portability, cost-effectiveness, high sensitivity, and superior selectivity make it a viable diabetes monitor. The biosensor's promising results show diabetes monitoring potential.

Piezoelectric biosensors

MIPs-based piezoelectric biosensors are formed by integrating MIPs with piezoelectric materials, which generate electrical signals in response to mechanical alterations.[64] Accurate analyte detection is achieved when target molecules bind to the MIPs layer, which causes a mass change that changes the resonance frequency of the biosensor. Commonly used biosensors in this industry include QCM.[92] Prior successes have proven that MIPs can be successfully integrated into QCM biosensors. It has also been reported in recent years that MIPs have found use in surface acoustic wave (SAW) biosensors. Environmental monitoring, clinical diagnostics, and food safety are some of the potential uses for these label-free, extremely sensitive biosensors that can be monitored in real time. Their functionality in complex sample matrices and resilience makes them useful in real-world applications.

By employing gram-negative and gram-positive bacteria, Tokonami and her colleagues were able to create bacterial templates on an overoxidized polypyrrole film.[77] These templates allowed for the exquisite molecular transfer of surface chemical structures. It just took minutes for the biosensor film to identify the target bacterium using a novel combination of dielectrophoresis. When tested on bacterial mixtures containing both gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) and gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) bacteria, the bacterial cavities demonstrated a high degree of selectivity for differentiating particular target bacteria.[77] The quick and specific recognition technique will open up new possibilities for the analysis of different species of bacteria and other microorganisms. In order to potentially diagnose hyperbilirubinemia, a condition characterized by an elevated blood bilirubin concentration that can cause irreversible brain damage or even death in infants, Çiçek et al. created a non-enzymatic bilirubin detection method using a QCM biosensor attached to a bilirubin-imprinted PHEMATrp polymeric film.[78] The gold surface of the QCM biosensor was modified by adding the bilirubin-imprinted PHEMATrp nanofilm to make it ready for use (Figure 2C). The QCM approach has been utilized to effectively detect bilirubin in aqueous solutions and healthy blood serum samples using the bilirubin-imprinted PHEMATrp-based biosensor in real-time. For the aqueous bilirubin solution, the quantitation limit

was determined to be 0.9 μg/mL and the detection limit to be 0.45 μg/mL.[78]

Applications in specific diseases

A biomarker is a measurable characteristic of the body or an indicator of a biologically induced change that is associated with a disease or health problem. There is a need for more rapid, efficient, and sensitive analytical procedures because results delays continue to cause a large number of deaths and illnesses.[93] Since MIPs are synthetic materials that may imitate biological recognition sufficiently to be referred to as plastic antibodies, they could be useful in resolving these challenges. The possibility that MIPs could offer a sensitive, quick, and inexpensive diagnostic tool has led to an upsurge in research into their use as a biomarker within the last decade.[94] Many diseases and conditions can be studied using MIPs as biomarkers. These include infectious diseases, bone loss, cardiovascular diseases, and many malignancies.

Cancer

Detecting cancer early is crucial for enhancing patient survival rates. By identifying cancer biomarkers, the disease can be diagnosed before it reaches a stage where treatment is no longer effective. Biomarkers can play a crucial role in tracking how well treatments and operations are working.[95] Recently, MIPs biosensors have captured interest in clinical settings because they are respond quickly, offer high specificity, and affordable. MIPs are not just limited to diagnostics; they have also been investigated for their role in targeted drug delivery.[94] This approach allows treatments to be released directly to cancer cells, which helps minimize side effects and enhances the effectiveness of the treatment. Their reliability and affordable production make them important resources in the progress of cancer theranostics.

Lin et al. developed a biosensor using surface-enhanced Raman spectroscopy (SERS) and surface molecularly imprinted polymer (SMIP) technology to quantify carcinoembryonic antigen (CEA), which is linked to various prevalent cancers.[76] SMIP imprints recognition sites with high affinity to the target of interest on SERS substrate, enabling more stable and specific capture. During quantitative analysis, they used an internal standard molecule to real-time correct Raman reporter signals. This assay achieves a LOD of 0.064 pg mL^{-1} with a detection range of 0.1 pg mL^{-1} to 10 μg mL^{-1}. This method even performed effectively for CEA detection in cancer patients' blood, suggesting biomarker-based cancer screening potential.[76] Another study introduced electrically-conducting poly(toluidine blue) as a synthetic receptor film, prepared through molecular imprinting and electrochemical methods, for detecting the breast cancer biomarker CA 15-3 [91]. The protein-imprinted film, grown on a pre-formed toluidine blue SAM at the AuSPE surface, enhanced the MIP's stability (Figure 3A). The MIP's binding affinity for CA 15-3 was significantly higher (~12-fold) than that of the non-imprinted particle (NIP) system, confirming the method's success. The biosensor displayed a linear response from 0.10 U mL^{-1} to 100 U mL^{-1}, with LOD below 0.10 U mL^{-1}, enabling clinically relevant biomarker detection in serum samples.[69] This approach offers a sensitive, rapid, and cost-effective method suitable for point-of-care screening.

Infectious diseases

Through the imprinting of whole viruses or specific protein indicators, MIPs are able to detect infectious diseases. Since viruses are easily identifiable by their unique shape, surface imprinting is a powerful tool for virus detection.[96] Improved sensitivity can be achieved using methods, such as core-shell imprinting, self-assembly, soft lithography, and bulk imprinting.[97] Despite their prevalence, surface-imprinted polymers are not very sensitive to electrochemistry due to their high electrical resistance. To overcome this, electrochemical biosensors can have conductive additives, such as nanocarbon compounds, added to them to boost their analytical signal.[98]

A MIPs-based electrochemical biosensor that can detect hepatitis C virus through its surface protein E2 was created by Antipchik et al.[72] The combination of green fluorescent protein with E2 helped stabilize the protein and prevent it from clumping together. To make the MIPs, an electrochemical imprinting process was used on an SPE electrode to imprint E2 onto poly(*m*-phenylenediamine). Because imprinting large proteins is so difficult, the surface imprinted polymer (SIP) method was employed since it provided better accessibility and binding kinetics. With a 15-min detection period and an LOD of 0.46 pg/mL, the biosensor showed promise for detecting chronic or early-stage hepatitis C.[72] Using MIPs for an inactivated strain of influenza A H5N1, Wangchareansak et al. investigated potential compounds that bind to the virus and suppress its activity through either allosteric or competitive processes.[79] By analyzing the conformational changes caused by interaction, they discovered that MIPs based on H5N1 could differentiate between probe molecules with high and low affinity[79] (Figure 3B). This approach has the potential to screen for inhibitors that cause conformational changes in target proteins, as the reduction in viral binding to the MIPs is directly proportional to the known binding constants. Proteins that provide therapeutic benefits through allosteric inhibition, such as HIV1-RT or EGFR, may benefit from this strategy.

Chronic diseases

MIPs hold great potential for detecting and managing chronic diseases, offering highly selective and sensitive biosensors for important biomarkers. For illnesses, including diabetes, heart disease, Alzheimer's, and chronic respiratory ailments, early detection, and vigilant monitoring are crucial for improving the treatment of patients.[93] MIPs-based biosensors are capable of identifying specific biomarkers like glucose for diabetes or troponins for heart disease, providing quick, and affordable screening options.[99] Their ability to remain stable and adapt to point-of-care applications makes MIPs important resources in managing long-term health conditions. Specifically, serious health issues include diabetes-related consequences including osteoporosis and decreased bone density. Risks of diabetes-induced bone loss can be reliably assessed with the use of MIP-based biosensors, which detect glucose levels and monitor relevant biomarkers. Biosensors that can detect troponins and other cardiac biomarkers can also be used in MIP applications for cardiovascular disorders, allowing for early detection and better patient outcomes.

Wardani and colleagues developed an electrochemical insulin biosensor that utilizes a gold electrode enhanced with

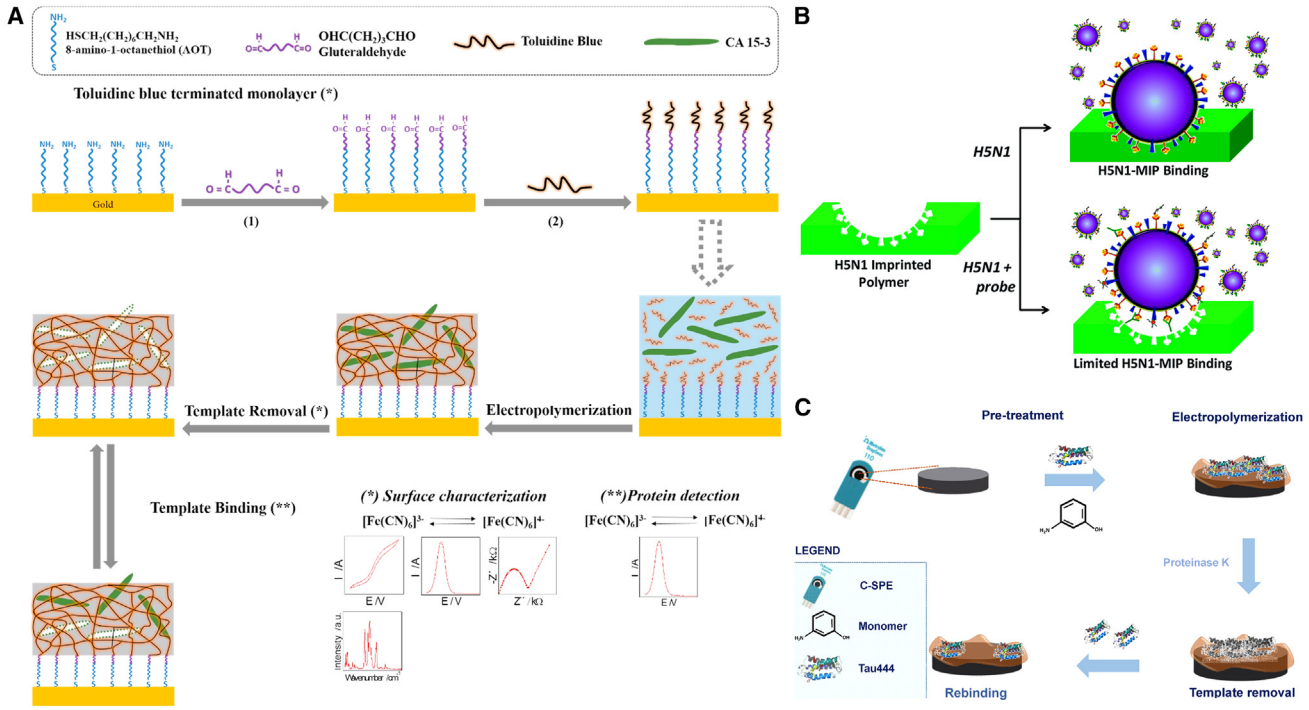

Figure 3. Schematic representations of MIP-based electrochemical biosensors for biomarker and virus detection

(A) Molecular imprinting and recognition concept of the MIP biosensor for CA 15-3 detection. (1) glutaraldehyde was applied to a premade AOT SAM on AuSPEs to create the Toluidine blue terminated monolayer, and (2) TB molecules were immobilized. Electropolymerization of TB retained the binding sites that were formed by the interaction of the functional monomer and the template. Rebinding empty voids are left behind after template removal. Using DPV (in the presence of a $[Fe(CN)_6]^{3-}/^{4-}$ redox probe), the final step involves the template rebinding to the binding sites, enabling the electrochemical detection of the protein by the constructed MIP electrode. Reproduced with permission from.[69]

(B) The H5N1 virus binds to a MIP, and the process is inhibited because the H5N1-probe complex undergoes a conformational shift. Reproduced with permission from.[79]

(C) Schematic depicting the electrochemically assisted MIP technique and the series of reactions that comprise the impedimetric transduction at C-SPEs for the tau protein measurement. Reproduced with permission from.[70]

carboxylated multiwalled carbon nanotubes (f-MWCNTs) and a MIP cryogel.[73] The MIPs offered specific recognition sites, and the macropores of the cryogel improved the transfer of insulin mass. The f-MWCNTs enhanced the biosensor's surface area and conductivity, which helped reduce the likelihood of insulin oxidation. This MIP cryogel/f-MWCNT biosensor demonstrated a linear detection range of 0.050–1.40 pM, with a limit of detection of 33 fM, exhibiting impressive selectivity and stability for as long as 10 weeks.[73] This presents a hopeful way to diagnose and monitor diabetes. A biosensor that utilizes a MIP has been created to identify Tau protein, which is an important biomarker for Alzheimer's disease. The MIP was developed by electropolymerizing 3-aminophenol on a carbon electrode, using p-Tau-441 as the template.[70] Once the template was removed, it offered selective binding sites (Figure 3C). The biosensor, capable of detecting as low as 0.02 pM, demonstrated impressive selectivity and functioned effectively in serum samples.[70] This platform provides a quick, affordable, and easy-to-use tool for on-site Tau protein screening, enhancing traditional clinical methods.

Imaging applications

Imaging techniques, together with molecular diagnostics, are critical in the fight against serious diseases. Particularly in multimodal techniques such as fluorescence/MRI, the use of fluorescent imaging is on the rise due to its many advantages, including lower prices, better resolution, and high molecular detection capabilities. It is critical to choose probes with excellent detection efficiency in MIP-based imaging. A wide range of imaging modalities have investigated the potential of biocompatible semiconductor QDs,[100] organic dye-doped polymers,[101] silica NPs, carbon nanodots, conjugated polymers, and materials, such as gold, silver, radioisotope-enriched, and iron oxide NPs.[102]

Kunath et al. created a plastic antibody that targets the terminal subunit, glucuronic acid (GlcA), of hyaluronan.[103] This compound is used as a biomarker for liver fibrosis and cirrhosis in chronic liver disease. They made dye-labeled GlcA-MIPs using an epitope method. Using epifluorescence and confocal microscopy, these MIPs were utilized to image hyaluronan on human keratinocytes and adult skin samples. A polymerizable rhodamine derivative was used for optical imaging, and the polymers

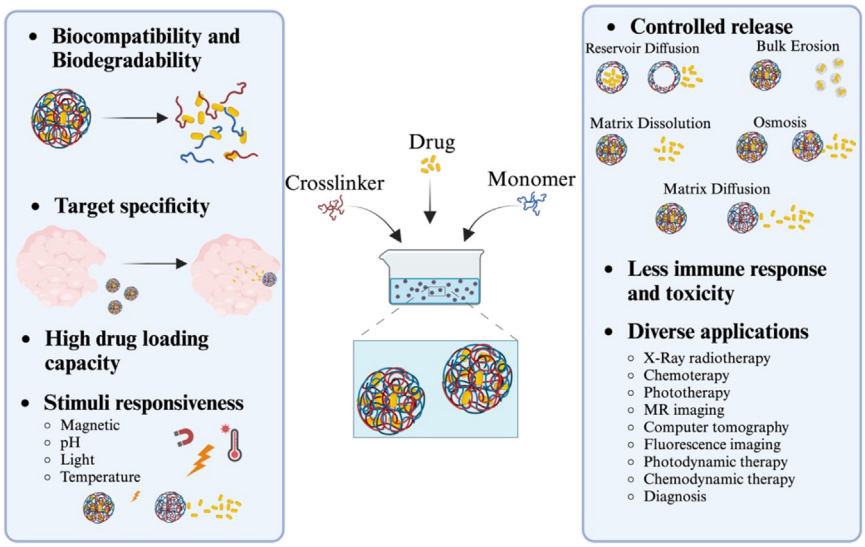

Figure 4. Schematic representation of MIP utilization as a drug carrier and advantages for therapeutic applications
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were based on previous work that used (N-acrylamido)-benzamidine (AAB) and methacrylamide (MAM) as monomers.[104] Using the same immunostaining methodology as MIPs, a reference method for hyaluronan localization was established using biotinylated hyaluronic acid-binding protein. Integrating dual-emission fluorescence MIPs (DE-MIPs) into a test strip for dopamine detection using colorimetric analysis allowed Wang et al. to develop a method for the identification of tiny biomolecules.[105] In order to diagnose neurological illnesses like schizophrenia and Parkinson's, dopamine is essential.[106] Red QDs quenched fluorescence upon dopamine binding, while blue dots maintained fluorescence in silica nanocores and blue dots in the polymer shell were used to construct DE-MIPs. The test strip's sensitivity and practicality for on-site diagnostics were demonstrated by its ability to detect dopamine in serum visually within 180 s, with a detection limit of 100–150 nM.

MOLECULAR IMPRINTING FOR THERAPY

The sophisticated design of MIPs makes their utilization advantageous for biosensing, diagnostic, imaging, and therapeutic (e.g., drug delivery systems (DDS)) applications. In this section, the general drug delivery mechanisms of MIPs were summarized as drug reservoirs, such as transdermal and oral applications, and targeted delivery for therapeutical approaches. Certain therapy techniques utilizing MIPs for cancer, and infectious diseases are also discussed.

Drug delivery systems

DDS refers to the approaches that carry and transport pharmaceutical substances through the body by enhancing the pharmacokinetic stages (absorption, distribution, metabolism, and excretion) of the drug.[107] In conventional drug release methods, low solubility, insufficient absorption, or toxic side effects due to the burst release phenomenon can be observed.[108] To minimize or completely overcome the mentioned negative effects, polymeric structures (e.g., coatings, hydrogels, micro-nano particles, scaffolds) are presented. They have high stability and resistance to extreme conditions such as high or low temperatures and pH, providing high protection to loaded drugs from enzymatic degradation in the biological environment. MIPs, also called artificial antibodies, are a special subtype of polymers targeting the receptor of the intended tissue area.[109] Even though there is no approved and commercial MIP-based DDS application, their reusability,[110] simple synthesis procedures,[111] and application of physical stimuli-responsive delivery mechanisms (light, temperature, electric field, etc.)[112] are promising for further research (Figure 4).

MIPs can be used as a drug reservoir for several applications.[113] Transdermal delivery is one of the areas combining MIPs utilization with traditional techniques.[114] Ruela et al. prepared nicotine MIPs with different polymerization methods and modified the transdermal patched with these MIPs for the controlled release of nicotine.[115,116] They optimized nicotine MIPs release kinetics with *in vitro* studies and successfully applied them to transdermal patches, reducing the burst release. Suedee and colleagues used MIPs assembled membranes for enantioselective-controlled delivery of β-blockers (S-propranolol) targeting one enantiomer of a chemical.[117–119] They investigated both synthetic monomers as methacrylic acid (MAA) and ethylene glycol dimethacrylate (EGDMA) for transdermal delivery[117] and bacterially derived cellulose[118] to enhance efficiency. Lastly, Brunella and coworkers compared non-molecularly and molecularly imprinted cyclodextrin-based nanosponges for the transdermal delivery of melatonin, a type of neurohormone.[120] They reported that binding sites on the MIP nanosponges provided selective and controllable melatonin release. MIPs did not lose their morphology or chemical stability by high temperatures during synthesis (140°C and 100°C) and were assessed as biocompatible, biodegradable, and non-toxic. Another MIP DDS application area is ocular therapeutics delivery to overcome the bioavailability and low drug loading capacity of ointments, solutions, and gels. In one of the pioneering articles, testosterone-added poly(2-hydroxyethyl methacrylate) (pHEMA) soft contact lenses were prepared to enhance testosterone release compared to water environments.[121] Mohajeri et al. presented brimonidine-imprinted hydrogel prepared with hydroxyethyl methacrylate (HEMA) as a backbone monomer, methacrylic acid (MAA), methacrylamide (MAAM) and 4-vinylpyridine (4VP),[122] and fluorometholone-imprinted MAA and HEMA based hydrogel soft contact lenses.[123] They showed better bioavailability and drug release profiles compared to NIP. Dorzolamide,[124] polymyxin B,[125] acyclovir (ACV), and its prodrug

valacyclovir (VACV)[126] are several types of drugs used for MIP-based ocular delivery.

MIPs have a high capacity to be used in targeted delivery systems by differentiating and binding the epitope of the special biomarkers. Traditionally, biologically originated molecules such as peptides and viruses are used as targeting ligands, however, they are costly, have limited stability and have short half-life. Replacing these with MIPs provides a highly selective, stimuli-responsive, controllable and sustainable release to the intended area as a "magic bullet".[127,128] Targeted delivery can be either passive or active. Passive targeting occurs via the enhanced permeability and retention (EPR) effect, where the vascularization abnormalities increase in the affected area. Even though MIP drug carriers can pass to the tumor site with the EPR effect easily, their circulation in the human body for a prolonged time causes aggregations on the other districts as well.[129] In active targeting, external stimuli (e.g., light, magnetism, pH) or internal stimuli (e.g., up-regulated and overexpressed receptor targeting at the infected tissue via antibodies) are necassary. The most important challenge here is the possible activation of the immune system due to the circulation of drugs with high concentrations to a specific area. To overcome this, the "trojan horse" mechanism is presented in that drug-loaded MIPs mimic the ligand/receptor area. When the ligand binds to the MIPs, drugs can be released.[130]

In addition to enhanced drug-loading capacity and controllable drug release kinetics, assessments of their biocompatibility are crucial for DDS and carriers. Long-term cytotoxic validation on MIPs as a drug carrier has been reported in various studies via *in vivo* studies by measuring the mice after MIP application or *in vitro* assessments with MTT assay.[22,131,132] Asadi and coworkers synthesized and used magnetic biodegradable MIPs, which showed no significant toxicity on the NIH/3T3 and HEK293 cell lines for 5 days of MTT results. They also utilized MIPs on rats for 72 h without any toxic effects.[131] In another study, MIPs were utilized to detect senescent cells by targeting B2M.[133] *in vivo* studies of nanoMIPs on mice indicated no significant effect on their overall health when administered orally, intraperitoneally, or intravenously over a 14-day follow-up post-treatment. The liver and kidney functions were also determined not to be changed. Furthermore, they observed these mice and evaluated them daily for distress indicators, which showed no alterations during the 14-day duration. Similarly, Zhang and colleagues used epitope-imprinted MIPs to target p32-positive tumor cells and deliver photodynamic therapy agents.[134] Epitope-imprinted MIPs were evaluated both *in vitro* by an MTT assay and *in vivo* in mice that showed no significant cytotoxicity. MIPs are promising tools for drug delivery in clinical applications, as indicated in the suggested articles with their biocompatible and non-toxic properties. However, the biocompatibility of the MIP is strongly dependent on the monomer and crosslinker. Moreover, a restricted number of studies have presented *in vivo* data for the assessment of MIP-based DDS. Thus, further research is required since it is a developing area at its early stage.[128]

Applications in cancer therapy

Cancer is one of the most vital diseases, and MIPs-based therapy applications, both *in vitro* and *in vivo*, are increasing each year. MIPs present alternative therapeutic methods owing to their capacity to selectively identify and adhere to certain cancer biomarkers, facilitating targeted drug administration and treatment with diverse approaches which could be (1) targeted drug delivery and sustained release, (2) synergistic therapies, (3) drug-free therapies, and their combinations.

In targeted delivery therapies, MIPs can be designed to selectively bind to the overexpressed cancer cell markers, facilitating selective administration of chemotherapeutic drugs.[135] This strategy can increase drug concentration in tumor sites while reducing the accumulation and adverse effects on healthy organs. In literature, overexpressed sialic acid (SA),[136,137] estimated glomerular filtration rate (EGFR),[51,138] human epidermal growth factor receptor 2 (HER2)[139] markers are also commonly targeted and studied elements for imprinting. The polymer network of MIPs can also be designed to degrade or release pharmaceutic cargo in accordance with particular stimuli, such as pH, light, or temperature variations inside the tumor microenvironment. One good example of this is the study by Suksuwan and colleagues, which utilized thermosensitive fluorescent particles (60–200 nm), produced from MAA, 2,6-bisacrylamide pyridine, and N-methylene bisacrylamide (NMBA) monomers, which were imprinted with thalidomide.[140] Upon the temperature beyond the lowest critical solution temperature, the particles selectively released the R-enantiomer of thalidomide, which inhibits the proliferation of cancer cells in the culture. In another study, Bărăian and colleagues worked on ruxolitinib (Rux) loaded MIPs for the therapy of glioblastoma, a type of central nervous system tumor.[141] Rux has a hydrophobic structure, and transferring Rux from the blood-brain barrier (BBB) is challenging. To address these problems, they loaded Rux in MIPs (Rux@MIP) and embedded particles in fibrin hydrogel to release in a controlled manner for a prolonged time.

Metal-organic frameworks (MOF), a class of metals with diverse subtypes as zeolitic imidazolate framework-8 (ZIF-8), zirconium 1,4-dicarboxybenzene (UiO-66) and copper benzene-1,3,5-tricarboxylate (HKUST-1), are commonly used stimuli-responsive materials for drug delivery and cancer therapy considering their high surface area, porous structure and modifiable features (fluorescent, thermal etc.).[142] When their material properties are combined with the high selectivity and targeting ability of MIPs, suitable concentrations of drugs can be delivered to the exact tumor area. For instance, under physical conditions, ZIF-8 is a non-toxic and stable type of MOF, but it is biodegradable in an acidic environment, including the tumor microenvironment. This feature of ZIF-8 provides pH-sensitive controlled release of drugs such as doxorubicin.[143,144] Song et al. reported ZIF-8/DOX-HA@MIP particles targeting sarcosine in prostate cancer (PCa) tissue cells.[144] They utilized hydrophilic hyaluronic acid to enhance drug loading capacity up to 88% and release kinetics. *In vitro* studies supported that these particles are successful in targeting the sarcosine molecule at the specific region. Han and coworkers worked on UiO-66 based doxorubicin (DOX) loaded MIPs (UiO-66-DOX@MIP) to target sialic acid.[145] They used dual-responsive strategies with both pH and glutathione (GSH) and observed that GSH significantly increased release property from 40% to 55%.

In synergistic therapy approaches, MIPs can be designed to improve therapeutic efficacy by the integration of various therapy modalities at once such as chemotherapeutic medicines and photosensitizers.[127,146] Liu et al. conducted a study about capsule-like MIPs that the DOX can be released with a chemo-photothermal method that assembles laser and lysozyme utilization.[127] They imprinted EGFR to target overexpressed tumor cells and encapsulated DOX in a zeolitic imidazolate framework-8 (ZIF-8) sacrificial layer to protect. Dopamine was chosen as the monomer, and during polymerization, ZIF-8 was etched, and DOX was encapsulated in polydopamine, which is a photo-thermal material providing controlled release of the drug. Shi and coworkers also used DOX as a template to produce silica-based MIPs and decorated their surface with cell-penetrating peptide (CPP) and aggregation-induced emission photosensitizer (TBTCP-CA).[32] They observed the synergistic usage of MIPs as scaffolds in photodynamic therapy significantly increased for cancer therapy. Theranostic approaches to molecular imprinting in cancer applications were detailed in current challenges and future perspectives.

Last but not least, MIPs can operate as therapeutic agents independent of medication delivery. They may inhibit tumor proliferation and migration by aiming and blocking certain recognition sites. Rangel et al. used MIP NPs to recognize and bind the epitope of classical type I cadherins, responsible for cell-cell adhesion and that play a critical role in maintaining tissue structure, integrity, and morphogenesis.[147] The MIP-NPs were found to damage the structure of the three-dimensional tumor models and hinder the invasion of HeLa ovarian cancer cells *in vitro*. Their results indicated that MIP-NPs possess significant potential in cancer therapy and diagnostics. In another study, human vascular endothelial growth factor (hVEGF), a powerful angiogenic agent that is essential for the growth of vascular endothelial cells, was used as a template for MIPs as an anti-angiogenesis agent.[148] The hVEGF is elevated in numerous cancers and is characterized by its role in tumor angiogenesis. Reducing the concentration of VEGF in the tumor microenvironment is a critical strategy for cancer treatment. Here, hVEGF-MIP targets the tumor site and binds substantial quantities of hVEGF. This binding lowers the quantity of free hVEGF in the tumor microenvironment, which inhibits angiogenesis and provides anti-tumor growth. In a similar application, HER2 glycans were used as a template for MIP-NP synthesis and HER2-dependent signaling processes were blocked by preventing HER2 heterodimerization.[149] This resulted in approximately 30% reduced HER2+ cell proliferation. Another novel study reported a fluorescent molecularly imprinted polymer (FMIP) to target the mitochondria in the cell and inhibit thymidylate synthase (TS), a key enzyme in DNA synthesis.[150] They utilized an amino acid sequence containing the active center of TS as the template, hindering DNA biosynthesis and thereby inhibiting tumor growth. *In vitro* experiments demonstrated that the mitochondria-targeted FMIP (Mito-FMIP) efficiently accumulated in mitochondria and inhibited CT26 cell proliferation by 59.9%. *In vivo* studies further showed that the tumor volume in the Mito-FMIP-treated group was only one-third of that in the untreated group.

Other therapeutic applications

MIPs therapy studies have been conducted in several different areas other than cancer applications, such as antimicrobial approaches. Mao et al. synthesized vancomycin (VA) loaded and pH-responsive nanosphere MIPs to coat the implants and prevent bacterial infections. Nano-sized particles enhanced the surface area and increased drug loading capacity. Compared to drug-loaded NIPs, MIPs showed significant antibacterial properties to *Staphylococcus aureus (S. aureus)* up to 92%.[151] In another study against bone infections, pH and thermal dual responsive and doxycycline (DOXY) imprinted particles were synthesized.[152] NIPAM monomer is used in addition to acrylamide to provide stimuli-responsive ability. Moreover, particles both had antibacterial effects against *E.coli* and *S. aureus*, and promoted bone regeneration. Elhabal and their study group made clindamycin imprinted MIP and immobilized these to polyurethane electrospun nanofibrous scaffolds for acne therapy.[153] They reported release rates of clindamycin, Clin-MIP, and Clin-MIP polyurethane nanofibers and indicated that nanofibrous structure is required for more sustained release. The literature also recorded levofloxacin,[154] and fenbufen[155] delivering MIPs to treat bacterial infections and inflammations. Blocking the ligand area of the harnessing agent with a bioreceptor is another approach. Researchers used this strategy against SARS-CoV-2 by synthesizing MIPs to selectively bind the receptor binding domain (RBD) of the virus and inhibit its binding to ACE-2.[156] These highly selective polymeric substances are named ‘‘monoclonal-type plastic antibodies’’.

In another MIPs-based therapy application, Rostamizadeh et al. employed naltrexone-loaded delivery vesicle MIPs and NIPs with two different monomers: acrylamide and methacrylic acid.[157] Naltrexone is used to treat addiction as a narcotic substance antagonist. This study showed that the monomer selection also may affect the release rate. Liu et al. aimed to develop a sustainable, biocompatible drug delivery system using titanium dioxide (TiO_2) and chitosan oligosaccharides for creating MIPs. Salidroside was determined as the target drug, which has low bioavailability, a short half-life, and a fast metabolism. The salidroside-based molecularly imprinted polymers (SDT-MIPs) demonstrated high drug-loading capacity, selective affinity, and effective, controlled release in simulated gastrointestinal conditions, showing potential for safe therapeutic use.[158]

Several applications of MIPs for chronic disease treatments were also reported in the literature. Tadi et al. presented MIPs tailored for pindolol (PDL), a beta-adrenergic receptor blocker, used to treat hypertension, cardiac arrhythmia, and angina pectoris.[159] Yu and coworkers developed an artificial recognition site for hypertension treatment with nanogel-based MIP (MIP-nanogel) designed to selectively recognize and neutralize angiotensins I and II.[160] Chronic inflammations also can be targeted and treated with MIPs. Costa and colleagues targeted inflamed tissue areas with MIPs that generally occurred after dental implantation.[161] They used folate (FT) imprinted polymers and biodegradable polycaprolactone (PCL) based polymer to deliver the cargo selectively to the inflamed tissue, considering the pH difference *in vitro* and *in vivo*. In another study, Soliman et al. studied rheumatoid arthritis, a chronic autoimmune disorder that causes inflammation and pain in joints.[162] They used a

magnetic core coated with mesoporous silica (Fe_2O_3@mSi), dopamine as a monomer, and methotrexate (MTX) as a drug loaded in the particles. They validated the drug-carrying MIPs efficiency with rat models by observing different parameters, such as paw diameter and animal weight. Histopathological findings and overall results showed that the treatment used by MIP is more efficient in reducing on-site inflammation than free MTX. Zhong and their group then developed core-shell MIP NPs capable of specifically recognizing, binding, and hydrolyzing interleukin-6 (IL-6), a key cytokine involved in cytokine release syndrome (CRS).[163] *In vivo* experiments demonstrated that these MIP NPs significantly reduced IL-6 levels and CRS symptoms. Compared to control groups, the MIP-treated subjects exhibited a more rapid and pronounced decrease in IL-6 concentrations, highlighting the potential of these NPs as therapeutic agents for conditions associated with elevated cytokine levels. Apart from these, MIPs were reported to sustain release of donepezil[164] and rivastigmine[165] for Alzheimer's disease, one of the most serious chronic neurodegenerative disorders.

THERANOSTIC APPLICATIONS OF MOLECULAR IMPRINTING

Molecular imprinting is a promising technique in theranostics, enabling the creation of selective recognition components that may concurrently assist in the diagnosis and treatment of several disorders. MIPs, with their synthetic receptors that mimic the binding properties of natural biological molecules, hold great promise in increasing the sensitivity, specificity and efficacy of theranostic platforms.[166] This section examines the integration of molecular imprinting into theranostic systems, focusing on its potential to revolutionize personalized medicine by providing targeted and responsive therapeutic solutions.

Direct monitoring of drug release and accumulation at specific sites throughout the application process is crucial for evaluating treatment efficacy. Theranostics, which combines diagnosis and treatment, is becoming more prevalent in imaging-guided DDS, especially in cancer therapies.[167] Theranostic MIPs offer the potential to function both as diagnostic and therapeutic agents. In these systems, MIPs are designed to recognize specific biomarkers for diagnostic purposes and subsequently trigger the release of therapeutic substances once the target is detected.[168] This dual functionality fits seamlessly with the objectives of precision medicine, which seeks to customize treatments according to the unique needs of each patient, informed by real-time diagnostic insights.[169] Moreover, MIPs provide a significant advantage for theranostic applications since their surface does not need modification with ligands and essentially contains particular binding sites.[51]

Accurately targeting cancer cells while concurrently enhancing the therapeutic efficiency of diverse treatments remains a significant challenge in contemporary medicine. A study created dual-template MIPs featuring a core-shell structure, whereby fluorescent silica NPs ($FSiO_2$) constitute the core and the MIPs layer forms the outer shell.[146] The printed layer was fabricated on the $FSiO_2$ surface using a free radical precipitation method, concurrently encapsulating gadolinium-doped silicon QDs (SiGdQDs) and photosensitizers (Ce6). In the polymerization process, two template molecules were included in the mixtures: the epitope of the CD59 protein (YNCPNPTADCK), which is overexpressed on the surface of most solid tumors, and the chemotherapeutic drug doxorubicin (DOX). Moreover, Ce6 included in NPs can generate cytotoxic singlet oxygen that effectively eradicates cancer cells upon 655 nm laser irradiation, facilitating synergistic cancer therapy when combined with encapsulated DOX. The incorporation of Ce6 and DOX into gadolinium-doped silicon QDs enables these manufactured MIPs to be utilized in targeted fluorescence imaging and MR imaging. The engineered MIPs can enhance the focused detection of biomarkers and facilitate precision therapy informed by cell imaging technologies. Another study presents an innovative approach to targeted cancer therapy using fluorescent zeolitic imidazolate framework-8 NPs (FZIF-8) loaded with DOX and coated with a MIP for enhanced tumor-targeting and drug delivery.[143] The MIP layer, imprinted with an epitope from the CD59 glycoprotein, selectively targets CD59-positive MCF-7 cancer cells, concentrating the NPs at the tumor site and enabling highly specific delivery (Figures 5A and 5B). Additionally, the MIP is engineered to degrade in response to tumor-specific stimuli high glutathione levels and acidic pH leading to precise DOX release directly in the tumor environment. *In vitro* experiments (Figure 5C) showed that FZIF-8/DOX-MIPs release DOX effectively under tumor-like circumstances with glutathione and acidic pH. With UV-vis spectroscopy, FZIF-8/DOX-MIPs demonstrated negligible DOX release in PBS without glutathione, showing stability in typical physiological settings due to the protective MIP layer that prevents premature drug release. As glutathione weakened the MIP shell, FZIF-8/DOX was exposed for targeted release, accelerating DOX release to 95% at pH 5.0 under mimicked tumor circumstances (10 mM GSH, pH 5.0 or 6.0). In Figure 5D, FZIF-8/DOX-MIPs have the maximum cytotoxicity in MCF-7 cells, which overexpress CD59, after 72 h, compared to LoVo cells with low CD59 expression and other control groups, including free DOX and NIPs. The selective targeting and prolonged release of DOX from FZIF-8/DOX-MIPs in CD59-positive MCF-7 cells confirms their targeted drug delivery and increased cytotoxicity. *In vitro* studies also confirmed that FZIF-8/DOX-MIPs are preferentially internalized by MCF-7 cells, while *in vivo* experiments showed substantial tumor growth inhibition in mouse models. The embedded carbon QDs further enhance the NPs function as fluorescent markers, supporting real-time imaging of tumor sites (Figure 5E). This dual-role NP system demonstrates high biocompatibility, precise targeting, effective drug release, and diagnostic utility, making it a compelling candidate for further research and potential applications in personalized cancer nanomedicine.

A new method for chemodynamic therapy (CDT) that improves targeted cancer cell treatment by autonomously generating hydrogen peroxide (H_2O_2) in the tumor microenvironment was established in another research.[170] Conventional CDT depends on the transformation of H_2O_2 into harmful hydroxyl radicals (OH) by Fenton or Fenton-like reactions; however, the restricted amounts of H_2O_2 in cancer cells may hinder its effectiveness. In this study, a degradable epitope-imprinted MIPs that autonomously produce H_2O_2, utilizing fluorescent calcium peroxide ($FCaO_2$) as both a source of H_2O_2 and an imaging probe were

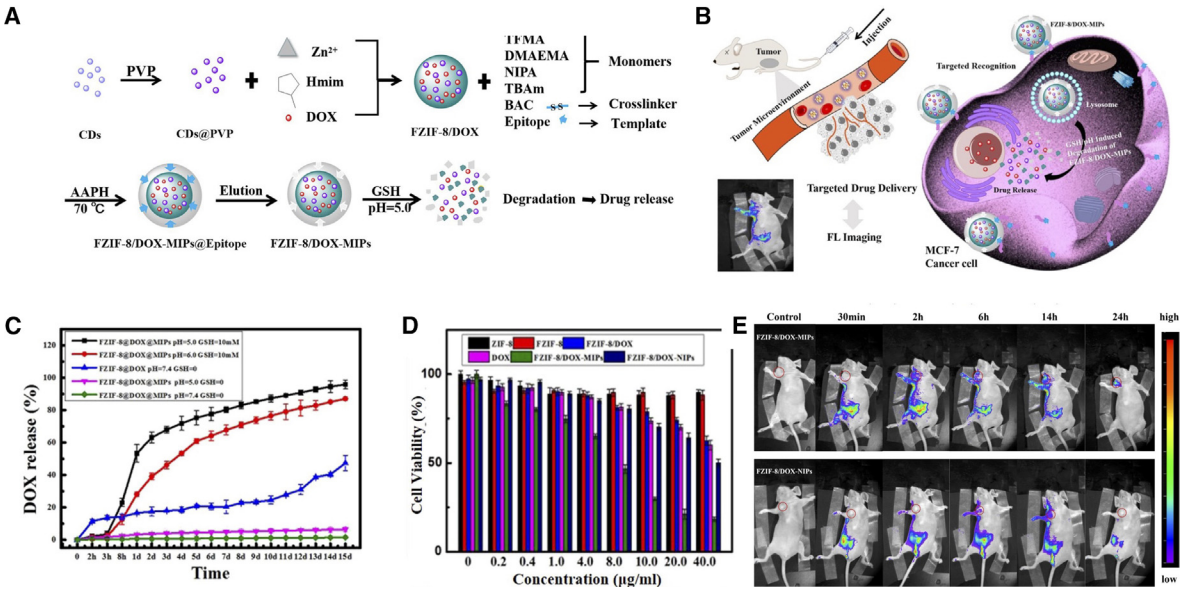

Figure 5. Design, drug release studies and in-vivo imaging of dual-responsive FZIF-8/DOX-MIP nanoparticles for targeted cancer therapy

(A) Synthesis process and glutathione/pH dual-responsive degradation pathway of FZIF-8/DOX-MIPs, (B) diagram illustrating targeted imaging and glutathione/pH-responsive drug release from FZIF-8/DOX-MIPs, (C) cumulative DOX release from nanoparticles under various conditions, (D) cell viability after 72-h incubation with different concentrations of nanoparticles (or equivalent DOX doses) and (E) fluorescence imaging of MCF-7 tumor-bearing mice at multiple time points following intraperitoneal injection with two types of nanoparticles (excitation at 530 nm). (Error bars represent the standard deviation of the mean data- $n = 8$, scale bar indicates the color scale from low to high values) Reproduced with permission from.[143]

prepared. The MIPs were synthesized using copper acrylate as a functional monomer and N,N′-bisacrylylcystamine (BAC) as a cross-linker, with a peptide from the extracellular region of CD47 serving as the imprint template for selective binding to CD47-positive cancer cells. This selectivity facilitated targeted fluorescence imaging and identification of cancer cells. In the tumor's mildly acidic, high-glutathione environment, the MIPs framework disintegrates, delivering $FCaO_2$, which interacts with water to perpetually generate H_2O_2. Copper ions in the MIPs facilitate a Fenton-like reaction, generating hydroxyl radicals that induce death in cancer cells. This MIP nano-platform offers a targeted CDT solution featuring accurate cancer cell identification, self-sustained H_2O_2 production, and regulated hydroxyl radical formation, thereby improving treatment effectiveness against CD47-positive malignancies.

Sunitinib (SUT) serves as a widely used tyrosine kinase inhibitor (TKI) in treating various cancers.[171] In another study explores SUT-selective MIPs which were developed by precipitation polymerization, using methacrylic acid (MAA) as a monomer and ethylene glycol dimethacrylate (EGDMA) as a crosslinker, followed by functionalization with the fluorescent marker rhodamine 6G through a radical grafting process involving hydrogen peroxide and ascorbic acid as redox agents[172] (Figure 6A). The dispersion at pH 5.4 demonstrated enhanced fluorescence emission compared to samples at pH 6.4 and 7.4, indicating the pH sensitivity of rhodamine 6G (R6G), a fluorochrome frequently utilized in theranostic applications. Figure 6B presents fluorescent microscopy pictures of R6G-grafted SUT-imprinted beads, illustrating their pH-responsive characteristics. The MIPs were characterized through adsorption isotherm and kinetic studies, with batch binding experiments confirming the presence of specific recognition sites within the polymer matrix that allowed selective binding to SUT. Adsorption data aligned well with the Langmuir model, while the kinetic profile of SUT binding followed a pseudo-first-order kinetic model for both imprinted and NIP. *In vitro* release studies demonstrated a controlled release pattern, with SUT release data fitting the Ritger-Peppas kinetic model, indicating a sustained release capability. Figure 6C shows SUT's burst, delay, and stable *in vitro* release characteristics from MIP and NIP particles. NIP particle burst release was 53% in the first 2 h, 92% at 6 h, and 97% at 24 h. The first release of MIP particles was 26%, rising to 67% at 6 h and 79% at 24 h. This controlled release from MIP particles is due to diffusion and imprinting, with selected recognition sites in the polymer interacting better with SUT molecules. SUT adsorption isotherms on MIP and NIP particles (Figure 6D) reveal that imprinted particles bind substantially more drug than non-imprinted ones. As the initial SUT concentration increased, both materials' adsorption capabilities increased until saturation. Semaxanib (SEM) at various doses was also tested for non-competitive binding and MIP cross-reactivity with a structural homologue of SUT (Figure 6E). These findings suggest that this SUT-imprinted polymer, combining the controlled release capabilities of MIPs with rhodamine 6G for real-time fluorescence imaging, has promising potential as a theranostic platform for simultaneous diagnosis and targeted cancer therapy.

A dual-template MIPs platform utilizing fluorescent silicon NPs (SiNPs) for targeted imaging and therapy in breast cancer was developed, incorporating a linear peptide sequence derived from the extracellular domain of human epidermal growth factor

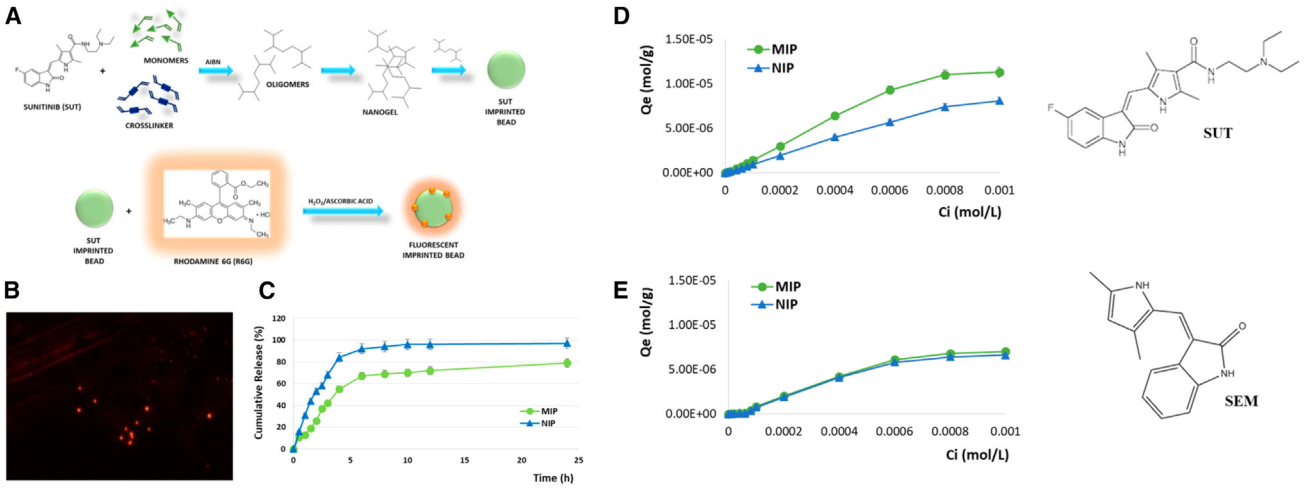

Figure 6. Synthesis, characterization and drug release performance of SUT-MIP fluorescent particles

(A) Synthesis of SUT imprinted beads functionalized with rhodamine 6G, (B) fluorescence microscopy image of rhodamine 6G grafted SUT imprinted particles, (C) cumulative release profiles of SUT from MIPs and NIPs. Adsorption isotherms for (D) SUT and (E) Semaxanib on both imprinted and non-imprinted particles. (Error bars represent the standard deviation of the mean data)Reproduced with permission from.[172]

receptor-2 (HER2) and containing DOX.[173] The MIP's epitope imprinting technique produced specific binding sites for HER2, facilitating precise targeting of HER2-positive breast cancer cells. The platform's excellent specificity for HER2-positive cells renders it appropriate for targeted fluorescence imaging, augmented by the robust emission characteristics of the SiNPs. Moreover, the DOX-loaded MIP serves as an effective therapeutic agent, preferentially targeting HER2-positive cells and triggering apoptosis. Fluorescence imaging revealed markedly enhanced NP uptake and intensified fluorescence in HER2-positive cells treated with the MIP, in contrast to those treated with NIP, while limited non-specific uptake was noted in HER2-negative and normal cells. Cell viability studies validated the targeted accumulation and efficient suppression of cancer cells by MIP@DOX.

The integration of molecular imprinting into theranostic platforms presents considerable potential for enhancing personalized therapy. MIPs can be engineered to detect disease signals unique to each patient, enabling the development of highly personalized diagnostic and treatment systems[174] (Table 2). Although the application of MIPs in diseases other than cancer is still limited by a lack of research, there is significant potential for its expansion. Common characteristics among diseases, such as cardiovascular diseases, diabetes, neurological disorders, and infections include the identification of specific biomarkers that could be targeted with MIP-based systems for both treatment and diagnosis. A disease biomarker can be utilized to functionalize NPs, facilitating targeted delivery and accumulation in pathological tissue.[175] For example, in cardiovascular diseases, carbon nanomaterials[176] and polymer-based materials[177] have been designed for theranostic applications. These diseases are characterized by pathological features such as low pH, elevated reactive oxygen species levels, abnormal enzyme activity, and lipid-rich necrotic cores. Such characteristics and biomarkers present opportunities for designing endogenous stimuli-responsive or targetable nanomedicines for both diagnosis and treatment. Leveraging these features, MIP-based systems can be tailored for advanced theranostic applications.[178] In diabetes, nanomaterials with precisely regulated properties[179–181] have evolved for the monitoring of blood glucose levels, as well as for the management and care of patients.[182] MIPs possess significant potential for enhancing theranostic applications in diabetes by combining highly sensitive glucose monitoring with intelligent DDS, hence facilitating more tailored and adaptive therapies.

Nanomaterials serve as effective theranostic agents in the treatment of neurological disorders such as Alzheimer's, Parkinson's, epilepsy, and Huntington's disease.[183] In infections, MIPs could function as sensors for detecting pathogens and could also be used to deliver targeted treatments like antibiotics or antivirals. Liposomes and NPs represent an attractive theranostic strategy for addressing microbial infections due to their chemical diversity in imaging applications and their ability to deliver antimicrobial agents.[184] The integration of therapeutic and diagnostic techniques may substantially enhance treatment efficacy by improving microbial targeting and monitoring capabilities during the treatment process, while demonstrating strong antimicrobial effects.[185] MIP-based devices in point-of-care settings facilitate real-time evaluation of disease progression and treatment efficacy, allowing for adjustments in therapy according to the changing requirements of patients. The incorporation of MIPs into theranostic devices facilitates the development of systems capable of diagnosing and treating diseases with enhanced precision, while simultaneously adapting in real time to optimize therapeutic results.

CURRENT CHALLENGES AND FUTURE PERSPECTIVES

Molecular imprinting shows great potential in theranostics, but there are still important challenges to overcome in order to fully

Table 2. MIP-integrated theranostic applications classified based on MIP structure, diagnostic mechanism, stimuli, and therapeutic outcome

MIP Structure	Diagnostic Mechanism	Stimuli	Therapeutic Outcome	Reference
$FSiO_2$ nanoparticle, SiGdQDs, DOX, and CD59 protein	Fluorescence Imaging	655 nm laser	Synergistic cancer therapy	Peng et al.[146]
FZIF-8 nanoparticle, carbon quantum dots, DOX, and CD59 glycoprotein		pH sensitive (5.0 or 6.0)	Targeted drug delivery	Qin et al.[143]
$FCaO_2$ nanoparticles, CD47 peptide epitope, copper acrylate, and BAC		pH sensitive (acidic)	CDT	Wang et al.[170]
SUT-imprinted polymer, rhodamine 6G, methacrylic acid, EGDMA		pH sensitive (6.4)	Cancer Therapy	Parisi et al.[172]
SiO_2 nanoparticles, HER2, and DOX		pH sensitive (5.5)	Cancer Therapy	Wang et al.[173]

realize its benefits. A significant challenge lies in the intricate task of imprinting large and structurally dynamic biomolecules, like proteins or nucleic acids.[186] The delicate nature and adaptable structure of these molecules can often result in challenges such as inconsistent binding site fidelity and lower recognition efficiency. To attain accurate and dependable imprinting for these targets, it is essential to investigate innovative strategies, including the development of novel functional monomers and the enhancement of polymerization techniques. The use of biosensing based on enzymes and antibodies at the point of care has greatly improved glucose monitoring for diabetics and pregnancy testing, among other medical applications, and has brought about significant cost savings, increased privacy, and ease of use. Due to their versatility, MIPs could bring comparable advantages to a broad variety of diseases and situations. This includes cancer biomarkers, infectious disease indicators, and inflammatory diseases. A great number of patents have been filed on MIPs worldwide, although the technology is still primarily limited to university facilities.[187] Despite this, the method will be transformative for both medical and environmental disciplines. Concerns with device design and fabrication as well as manufacturing scale up have slowed the commercialization of MIPs technology from its inception in the lab. While most of the present study has focused on capturing the target molecule from different and complex matrices, an effective device should also offer the user a way to interpret and store the measured data.[188] The ideal system would be compact, easily transportable, simple to operate, quick, and inexpensive. Interfaces enabling smart phones to work with MIPs-based biosensors for diagnostics/analysis platforms have been proposed, and recent improvements in electronics and optical interfaces have helped solve this challenge. Full development of a calibrated MIP-based system is still in its early stages and will necessitate substantial investment in research.[188,189]

Alongside these scientific problems, practical obstacles to the clinical implementation of molecular imprinting technology must also be resolved. A major concern is the lack of a standardized quality control (QC) system specifically designed for MIPs.[190] In the absence of such a system, maintaining the constant performance, sensitivity, and specificity of MIPs proves difficult. Establishing effective QC methods entails standardizing polymerization protocols, confirming template removal processes to maintain binding site integrity, and employing real-time monitoring during production to identify anomalies. Methods such as Fourier transform infrared spectroscopy (FTIR) and NMR facilitate repeatability, while sophisticated techniques like SPR and QCM can assess binding efficiency in clinical settings.[191,192] Implementing a QC framework will facilitate the transition from laboratory-scale MIP development to scalable clinical use.

Cost-benefit analysis is a crucial element in the clinical implementation of MIPs. Although the early expenses of constructing MIP-based systems may be substantial, these expenditures are mitigated by their long-term advantages. MIPs utilize synthetic components rather than biological materials, such as antibodies, rendering them more resilient, and cost-effective to manufacture.[102] Batch production and automation may further decrease expenses, facilitating the development of cost-effective diagnostic equipment that operates dependably in various clinical environments. Moreover, by delivering expedited and precise diagnostics, MIPs could contribute to a reduction in overall healthcare expenditures by facilitating early disease identification and diminishing dependence on more invasive or costly interventions.

Even with these obstacles, the outlook for molecular imprinting in theranostics looks promising.[193] New studies are exploring hybrid materials that blend MIPs with nanomaterials like metal NPs or graphene, aiming to boost sensitivity and functional versatility. These hybrid systems could really enhance how diagnostic devices work and improve drug delivery platforms. Moreover, incorporating artificial intelligence (AI) and ML into MIPs design and optimization has the potential to transform the field, allowing for the swift creation of highly effective recognition elements customized for particular clinical requirements. A potential domain is the investigation of intelligent, stimuli-responsive MIPs that can modify their characteristics in reaction to alterations in the biological milieu. These innovative materials may facilitate the development of dynamic theranostic systems that adjust to various disease states or therapy phases, providing unmatched precision in personalized medicine. In conclusion, although molecular imprinting

technology encounters challenges that must be addressed, continuous progress facilitates its broader application in theranostics. Collaborative efforts across chemists, biologists, engineers, and data scientists will be essential to surmount existing constraints and unveil new opportunities in illness management. Molecular imprinting is set to emerge as a fundamental technique in the forthcoming era of customized medicine as research advances.

DISCUSSION

Molecular imprinting technology, particularly through the innovative applications of MIPs, has emerged as a transformative tool in the fields of diagnostics and therapeutics. Integrating MIPs into theranostic platforms offers unparalleled specificity and sensitivity, enabling a promising approach for personalized medicine that combines diagnostic and therapeutic capabilities. This dual functionality is particularly impactful in managing complex diseases, such as cancer, infectious diseases, and chronic conditions, where the need for precise detection and targeted treatment is paramount. Through advancements in the development of biosensors and targeted DDS, MIPs have shown remarkable potential in enhancing diagnostic accuracy and therapeutic efficacy, offering clinicians tools that can both identify and respond to disease states in real time. On the other hand, despite these advancements, there are still significant challenges in translating MIPs from research to clinical applications. The encounters, such as biocompatibility, stability in biological environments, scalability of production, and regulatory issues need to be addressed to ensure that MIPs can meet the stringent requirements in medical practice. Future research needs to focus on refining these aspects to pave the way for MIPs to be incorporated into next-generation medical devices and treatments. As the field progresses, the ability of MIPs to offer precise, responsive, and patient-specific interventions has considerable potential to revolutionize healthcare, paving the way for highly personalized and efficient medical solutions. In sum, molecular imprinting technology not only advances theranostic capabilities but also stands at the forefront of innovation, promising a future in which medical interventions are seamlessly tailored to the unique needs of personalized medicine.

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AUTHOR CONTRIBUTIONS

E.G.Y.: conceptualization, writing—original draft, writing—review and editing; B.N.K.: conceptualization, writing—original draft, review and editing; Y.A.: conceptualization, writing—original draft, review and editing; Ö.E.: conceptualization, writing—original draft, review and editing; Y.S.: writing—original draft, review and editing, supervision; F.I.: writing—review and editing, supervision; A.D.: writing—review and editing, supervision.

DECLARATION OF INTERESTS

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

REFERENCES

1. Seidlin, S.M., Marinelli, L.D., and Oshry, E. (1990). Radioactive iodine therapy: Effect on functioning metastases ofadenocarcinoma of the thyroid. CA Cancer J. Clin. *40*, 299–317. https://doi.org/10.3322/canjclin.40.5.299.
2. Herrmann, K., Schwaiger, M., Lewis, J.S., Solomon, S.B., McNeil, B.J., Baumann, M., Gambhir, S.S., Hricak, H., and Weissleder, R. (2020). Radiotheranostics: a roadmap for future development. Lancet Oncol. *21*, e146–e156. https://doi.org/10.1016/S1470-2045(19)30821-6.
3. Zhang, Z., Kang, M., Tan, H., Song, N., Li, M., Xiao, P., Yan, D., Zhang, L., Wang, D., and Tang, B.Z. (2022). The fast-growing field of photo-driven theranostics based on aggregation-induced emission. Chem. Soc. Rev. *51*, 1983–2030. https://doi.org/10.1039/D1CS01138C.
4. Cheng, X., Gao, J., Ding, Y., Lu, Y., Wei, Q., Cui, D., Fan, J., Li, X., Zhu, E., Lu, Y., et al. (2021). Multi-functional liposome: A powerful theranostic nano-platform enhancing photodynamic therapy. Adv. Sci. *8*, 2100876. https://doi.org/10.1002/advs.202100876.
5. Huang, P., Wang, C., Deng, H., Zhou, Y., and Chen, X. (2023). Surface engineering of nanoparticles toward cancer theranostics. Acc. Chem. Res. *56*, 1766–1779. https://doi.org/10.1002/advs.202100876.
6. Haupt, K., Medina Rangel, P.X., and Bui, B.T.S. (2020). Molecularly imprinted polymers: Antibody mimics for bioimaging and therapy. Chem. Rev. *120*, 9554–9582. https://doi.org/10.1021/acs.chemrev.0c00428.
7. Jenkins, A.L., Yin, R., and Jensen, J.L. (2001). Molecularly imprinted polymer sensors for pesticide and insecticide detection in water. Analyst *126*, 798–802. https://doi.org/10.1039/B008853F.
8. Wu, X., Cao, J., Bao, S., Shao, G., Wang, Z., Qin, B., Wang, T., and Fu, Y. (2021). Preparation and application of modified three-dimensional cellulose microspheres for paclitaxel targeted separation. J. Chromatogr. A *1655*, 462487. https://doi.org/10.1016/j.chroma.2021.462487.
9. Beyazit, S., Tse Sum Bui, B., Haupt, K., and Gonzato, C. (2016). Molecularly imprinted polymer nanomaterials and nanocomposites by controlled/living radical polymerization. Prog. Polym. Sci. *62*, 1–21. https://doi.org/10.1016/j.progpolymsci.2016.04.001.
10. Zhang, H. (2020). Molecularly imprinted nanoparticles for biomedical applications. Adv. Mater. *32*, 1806328. https://doi.org/10.1002/adma.201806328.
11. Cieplak, M., and Kutner, W. (2016). Artificial biosensors: How can molecular imprinting mimic biorecognition? Trends Biotechnol. *34*, 922–941. https://doi.org/10.1016/j.tibtech.2016.05.011.
12. Pirzada, M., Sehit, E., and Altintas, Z. (2020). Cancer biomarker detection in human serum samples using nanoparticle decorated epitope-mediated hybrid MIP. Biosens. Bioelectron. *166*, 112464. https://doi.org/10.1016/j.bios.2020.112464.
13. Chen, W., Ma, Y., Pan, J., Meng, Z., Pan, G., and Sellergren, B. (2015). Molecularly imprinted polymers with stimuli-responsive affinity: Progress and perspectives. Polymers *7*, 1689–1715. https://doi.org/10.3390/polym7091478.
14. Arshady, R., and Mosbach, K. (1981). Synthesis of substrate-selective polymers by host-guest polymerization. Die Makromol. Die Chem. (Berl.) *182*, 687–692. https://doi.org/10.1002/macp.1981.021820240.
15. Chianella, I., Lotierzo, M., Piletsky, S.A., Tothill, I.E., Chen, B., Karim, K., and Turner, A.P.F. (2002). Rational design of a polymer specific for

microcystin-LR using a computational approach. Anal. Chem. *74*, 1288–1293. https://doi.org/10.1021/ac010840b.

16. De Middeleer, G., Dubruel, P., and De Saeger, S. (2016). Characterization of MIP and MIP functionalized surfaces: Current state-of-the-art. TrAC Trends Anal. Chem. *76*, 71–85. https://doi.org/10.1016/j.trac.2015.11.007.
17. Çimen, D., Bereli, N., and Denizli, A. (2023). Molecularly imprinted surface plasmon resonance sensor-based devices for clinical applications. Biomed. Mater. Devices *1*, 202–212. https://doi.org/10.1007/s44174-022-00022-3.
18. Boysen, R.I. (2019). Advances in the development of molecularly imprinted polymers for the separation and analysis of proteins with liquid chromatography. J. Sep. Sci. *42*, 51–71. https://doi.org/10.1002/jssc.201800945.
19. Dakova, I., Karadjova, I., Ivanov, I., Georgieva, V., Evtimova, B., and Georgiev, G. (2007). Solid phase selective separation and preconcentration of Cu(II) by Cu(II)-imprinted polymethacrylic microbeads. Anal. Chim. Acta *584*, 196–203. https://doi.org/10.1016/j.aca.2006.10.050.
20. Yilmaz, F., Bereli, N., Derazshamshir, A., Çimen, D., Akgönüllü, S., Saylan, Y., Topçu, A.A., and Denizli, A. (2020). Molecularly Imprinted Sensors for Detecting Controlled Release of Pesticides. In Controlled Release of Pesticides for Sustainable Agriculture, S. Thomas, T. Volova, K.R. Rakhimol, and K. Jayachandran, eds. (Springer International Publishing), pp. 207–235. https://doi.org/10.1007/978-3-030-23396-9_9.
21. Say, R., Ersöz, A., and Denizli, A. (2003). Selective separation of uranium containing glutamic acid molecular-imprinted polymeric microbeads. Sep. Sci. Technol. *38*, 3431–3447. https://doi.org/10.1081/SS-120023407.
22. He, S., Zhang, L., Bai, S., Yang, H., Cui, Z., Zhang, X., and Li, Y. (2021). Advances of molecularly imprinted polymers (MIP) and the application in drug delivery. Eur. Polym. J. *143*, 110179. https://doi.org/10.1016/j.eurpolymj.2020.110179.
23. Saylan, Y., Erdem, Ö., Inci, F., and Denizli, A. (2020). Advances in biomimetic systems for molecular recognition and biosensing. Biomimetics *5*, 20. https://doi.org/10.3390/biomimetics5020020.
24. Saylan, Y., Gerdan, Z., Çalışır, M., and Denizli, A. (2024). Chapter 11 - Nanomolecular imprinted templates for virus detection. In Biophysics At the Nanoscale, A. Denizli, ed. (Academic Press), pp. 203–232. https://doi.org/10.1016/B978-0-443-15359-4.00007-3.
25. Zhou, J., Cheng, X., Guo, Z., Ali, M.M., Zhang, G., Tao, W.A., Hu, L., and Liu, Z. (2023). Epitope imprinting of phospholipids by oriented assembly at the oil/water interface for the selective recognition of plasma membranes. Angew. Chemie *62*, e202213938. https://doi.org/10.1002/ange.202213938.
26. Zhao, Q., Cheng, X., Hu, S., Zhao, M., Chen, J., Mu, M., Yang, Y., Liu, H., Hu, L., Zhao, B., and Song, W. (2024). Bilateral efforts to improve SERS detection efficiency of exosomes by Au/$Na_7PMo_{11}O_{39}$ combined with phospholipid epitope imprinting. Biosens. Bioelectron. *258*, 116349. https://doi.org/10.1016/j.bios.2024.116349.
27. Liu, H., Jin, P., Zhu, F., Nie, L., and Qiu, H. (2021). A review on the use of ionic liquids in preparation of molecularly imprinted polymers for applications in solid-phase extraction. TrAC Trends Anal. Chem. *134*, 116132. https://doi.org/10.1016/j.trac.2020.116132.
28. Song, Z., Li, J., Lu, W., Li, B., Yang, G., Bi, Y., Arabi, M., Wang, X., Ma, J., and Chen, L. (2022). Molecularly imprinted polymers based materials and their applications in chromatographic and electrophoretic separations. TrAC Trends Anal. Chem. *146*, 116504. https://doi.org/10.1016/j.trac.2021.116504.
29. Li, P., Pang, J., Xu, S., He, H., Ma, Y., and Liu, Z. (2022). A glycoform-resolved dual-modal ratiometric immunoassay improves the diagnostic precision for hepatocellular carcinoma. Angew. Chem. Int. Ed. Engl. *61*, e202113528. https://doi.org/10.1002/anie.202113528.
30. Zhang, H. (2014). Water-compatible molecularly imprinted polymers: Promising synthetic substitutes for biological receptors. Polymer. *55*, 699–714. https://doi.org/10.1016/j.polymer.2013.12.064.
31. Song, Q., Li, Y., Ma, L., Li, Y., and Lv, Y. (2024). A high-throughput screening strategy for synthesizing molecularly imprinted polymer nanoparticles selectively targeting tumors. Adv. Healthc. Mater. *13*, 2400290. https://doi.org/10.1002/adhm.202400290.
32. Shi, H., Wan, Y., Tian, X., Wang, L., Shan, L., Zhang, C., Wu, M.Y., and Feng, S. (2022). Synergistically enhancing tumor chemotherapy using an aggregation-induced emission photosensitizer on covalently conjugated molecularly imprinted polymer nanoparticles. ACS Appl. Mater. Interfaces *14*, 56585–56596. https://doi.org/10.1021/acsami.2c17731.
33. Ye, L., Cormack, P.A.G., and Mosbach, K. (1999). Molecularly imprinted monodisperse microspheres for competitive radioassay. Anal. Commun. *36*, 35–38. https://doi.org/10.1039/A809014I.
34. Fang, L., Chen, S., Guo, X., Zhang, Y., and Zhang, H. (2012). Azobenzene-containing molecularly imprinted polymer microspheres with photo-and thermoresponsive template binding properties in pure aqueous media by atom transfer radical polymerization. Langmuir *28*, 9767–9777. https://doi.org/10.1021/la301314w.
35. Bhogal, S., Kaur, K., Malik, A.K., Sonne, C., Lee, S.S., and Kim, K.H. (2020). Core-shell structured molecularly imprinted materials for sensing applications. TrAC Trends Anal. Chem. *133*, 116043. https://doi.org/10.1016/j.trac.2020.116043.
36. Çakir, P., Cutivet, A., Resmini, M., Bui, B.T.S., and Haupt, K. (2013). Protein-size molecularly imprinted polymer nanogels as synthetic antibodies, by localized polymerization with multi-initiators. Adv. Mater. *25*, 1048–1051. https://doi.org/10.1002/adma.201203400.
37. Tse Sum Bui, B., Auroy, T., and Haupt, K. (2022). Fighting antibiotic-resistant bacteria: Promising strategies orchestrated by molecularly imprinted polymers. Angew. Chem. Int. Ed. Engl. *61*, e202106493. https://doi.org/10.1002/anie.202106493.
38. Zhang, Y., Li, S., Ma, X.T., He, X.W., Li, W.Y., and Zhang, Y.K. (2020). Carbon dots-embedded epitope imprinted polymer for targeted fluorescence imaging of cervical cancer via recognition of epidermal growth factor receptor. Microchim. Acta *187*, 228. https://doi.org/10.1007/s00604-020-4198-7.
39. Amatatongchai, M., Thimoonnee, S., Jarujamrus, P., Nacapricha, D., and Lieberzeit, P.A. (2020). Novel amino-containing molecularly-imprinted polymer coating on magnetite-gold core for sensitive and selective carbofuran detection in food. Microchem. J. *158*, 105298. https://doi.org/10.1016/j.microc.2020.105298.
40. Cui, Y., Ding, L., and Ding, J. (2022). Recent advances of magnetic molecularly imprinted materials: From materials design to complex sample pretreatment. TrAC Trends Anal. Chem. *147*, 116514. https://doi.org/10.1016/j.trac.2021.116514.
41. Azargoshasb, T., Parvizi, R., Bozorgzadeh, F., Navid, H.A., and Heidari, H. (2023). Smart green CQD@ SiO_2 hybrid coated optical fiber manifesting dual versatile absorptive and MIP features towards epinephrine detection. Nanoscale Adv. *5*, 459–470. https://doi.org/10.1039/D2NA00687A.
42. Orbay, S., Kocaturk, O., Sanyal, R., and Sanyal, A. (2022). Molecularly imprinted polymer-coated inorganic nanoparticles: Fabrication and biomedical applications. Micromachines *13*, 1464. https://doi.org/10.3390/mi13091464.
43. Unger, C., and Lieberzeit, P.A. (2021). Molecularly imprinted thin film surfaces in sensing: Chances and challenges. React. Funct. Polym. *161*, 104855. https://doi.org/10.1016/j.reactfunctpolym.2021.104855.
44. Su, H., Ren, H., Maimaitikelimu, X., Xu, J., Bian, F., and Wang, H. (2024). Molecularly and ionically imprinted polymers-based chemical sensors in chemical assays. Chem. Eng. J. *499*, 156315. https://doi.org/10.1016/j.cej.2024.156315.

45. Liu, Y., Wang, L., Li, H., Zhao, L., Ma, Y., Zhang, Y., Liu, J., and Wei, Y. (2024). Rigorous recognition mode analysis of molecularly imprinted polymers—Rational design, challenges, and opportunities. Prog. Polym. Sci. *150*, 101790. https://doi.org/10.1016/j.progpolymsci.2024.101790.

46. Sobiech, M., and Luliński, P. (2024). Molecularly imprinted solid phase extraction–recent strategies, future prospects and forthcoming challenges in complex sample pretreatment process. TrAC Trends Anal. Chem. *174*, 117695. https://doi.org/10.1016/j.trac.2024.117695.

47. Quezada, C., Samhitha, S.S., Salas, A., Ges, A., Barraza, L.F., Blanco-López, M.C., Solís-Pomar, F., Pérez-Tijerina, E., Medina, C., and Meléndrez, M. (2024). Sensors based on molecularly imprinted polymers in the field of cancer biomarker detection: A review. Nanomaterials *14*, 1361. https://doi.org/10.3390/nano14161361.

48. Kumar, A., Kashyap, S., Mazahir, F., Sharma, R., and Yadav, A.K. (2024). Unveiling the potential of molecular imprinting polymer-based composites in the discovery of advanced drug delivery carriers. Drug Discov. Today *29*, 104164. https://doi.org/10.1016/j.drudis.2024.104164.

49. Karasu, T., Çalışır, F., Pişkin, S., Özgür, E., Armutcu, C., Çorman, M.E., and Uzun, L. (2024). An intriguing future is approaching: Artificial intelligence meets molecularly imprinted polymers. J. Pharm. Biomed. Anal. Open *4*, 100041. https://doi.org/10.1016/j.jpbao.2024.100041.

50. Ding, L., Agrawal, P., Singh, S.K., Chhonker, Y.S., Sun, J., and Murry, D.J. (2024). Polymer-based drug delivery systems for cancer therapeutics. Polymers *16*, 843. https://doi.org/10.3390/polym16060843.

51. Kang, M.S., Cho, E., Choi, H.E., Amri, C., Lee, J.-H., and Kim, K.S. (2023). Molecularly imprinted polymers (MIPs): emerging biomaterials for cancer theragnostic applications. Biomater. Res. *27*, 45. https://doi.org/10.1186/s40824-023-00388-5.

52. Wang, L., Pagett, M., and Zhang, W. (2023). Molecularly imprinted polymer (MIP) based electrochemical sensors and their recent advances in health applications. Sens. Actuat. Rep. *5*, 100153. https://doi.org/10.1016/j.snr.2023.100153.

53. Ni, X., Tang, X., Wang, D., Zhang, J., Zhao, L., Gao, J., He, H., and Dramou, P. (2023). Research progress of sensors based on molecularly imprinted polymers in analytical and biomedical analysis. J. Pharm. Biomed. Anal. *235*, 115659. https://doi.org/10.1016/j.jpba.2023.115659.

54. Ramajayam, K., Ganesan, S., Ramesh, P., Beena, M., Kokulnathan, T., and Palaniappan, A. (2023). Molecularly imprinted polymer-based biomimetic systems for sensing environmental contaminants, biomarkers, and bioimaging applications. Biomimetics *8*, 245. https://doi.org/10.3390/biomimetics8020245.

55. Suzaei, F.M., Daryanavard, S.M., Abdel-Rehim, A., Bassyouni, F., and Abdel-Rehim, M. (2023). Recent molecularly imprinted polymers applications in bioanalysis. Chem. Zvesti *77*, 619–655. https://doi.org/10.1007/s11696-022-02488-3.

56. Li, Y., Guan, C., Liu, C., Li, Z., and Han, G. (2024). Disease diagnosis and application analysis of molecularly imprinted polymers (MIPs) in saliva detection. Talanta *269*, 125394. https://doi.org/10.1016/j.talanta.2023.125394.

57. Wu, L., Li, X., Miao, H., Xu, J., and Pan, G. (2022). State of the art in development of molecularly imprinted biosensors. VIEW *3*, 20200170. https://doi.org/10.1002/VIW.20200170.

58. Li, G. (2018). Nano-inspired Biosensors for Protein Assay with Clinical Applications, 1st ed. (Elsevier). https://doi.org/10.1016/C2016-0-01779-5.

59. Xu, J., Miao, H., Wang, J., and Pan, G. (2020). Molecularly imprinted synthetic antibodies: from chemical design to biomedical applications. Small *16*, 1906644. https://doi.org/10.1002/smll.201906644.

60. Ovezova, M., Yılmaz, F., Göktürk, I., Güler, K.Ç., and Denizli, A. (2024). Molecularly imprinted polymers for pharmaceutical and biomedical analysis. J. Pharm. Biomed. Anal. Open *4*, 100038. https://doi.org/10.1016/j.jpbao.2024.100038.

61. Carballido, L., Karbowiak, T., Cayot, P., Gerometta, M., Sok, N., and Bou-Maroun, E. (2022). Applications of molecularly imprinted polymers and perspectives for their use as food quality trackers. Chem *8*, 2330–2341. https://doi.org/10.1016/j.chempr.2022.05.021.

62. Akgönüllü, S., and Denizli, A. (2023). Molecular imprinting-based sensors: Lab-on-chip integration and biomedical applications. J. Pharm. Biomed. Anal. *225*, 115213. https://doi.org/10.1016/j.jpba.2022.115213.

63. Saylan, Y., Kılıç, S., and Denizli, A. (2024). Biosensing applications of molecularly imprinted-polymer-based nanomaterials. Processes *12*, 177. https://doi.org/10.3390/pr12010177.

64. Rajpal, S., and Mishra, P. (2022). Next generation biosensors employing molecularly imprinted polymers as sensing elements for in vitro diagnostics. Biosens. Bioelectron. X *11*, 100201. https://doi.org/10.1016/j.biosx.2022.100201.

65. Siavashy, S., Soltani, M., Rahimi, S., Hosseinali, M., Guilandokht, Z., and Raahemifar, K. (2024). Recent advancements in microfluidic-based biosensors for detection of genes and proteins: Applications and techniques. Biosens. Bioelectron. X *19*, 100489. https://doi.org/10.1016/j.biosx.2024.100489.

66. Erdem, Ö., Yilmaz, E., Küçük, B., Inci, F., and Saylan, Y. (2024). Microfluidic-Based Plasmonic Nanosensors for Biological and Chemical Threats. In Plasmonic Nanosensors for Biological and Chemical Threats (CRC Press), pp. 91–117. https://doi.org/10.1201/9781003459316-5.

67. Yarman, A., Kurbanoglu, S., Jetzschmann, K.J., Ozkan, S.A., Wollenberger, U., and Scheller, F.W. (2018). Electrochemical MIP-sensors for drugs. Curr. Med. Chem. *25*, 4007–4019. https://doi.org/10.2174/0929867324666171005103712.

68. Raziq, A., Kidakova, A., Boroznjak, R., Reut, J., Öpik, A., and Syritski, V. (2021). Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. Biosens. Bioelectron. *178*, 113029. https://doi.org/10.1016/j.bios.2021.113029.

69. Ribeiro, J.A., Pereira, C.M., Silva, A.F., and Sales, M.G.F. (2018). Disposable electrochemical detection of breast cancer tumour marker CA 15-3 using poly(Toluidine Blue) as imprinted polymer receptor. Biosens. Bioelectron. *109*, 246–254. https://doi.org/10.1016/j.bios.2018.03.011.

70. Ben Hassine, A., Raouafi, N., and Moreira, F.T.C. (2021). Novel electrochemical molecularly imprinted polymer-based biosensor for Tau protein detection. Chemosensors *9*, 238. https://doi.org/10.3390/chemosensors9090238.

71. Liustrovaite, V., Pogorielov, M., Boguzaite, R., Ratautaite, V., Ramanaviciene, A., Pilvenyte, G., Holubnycha, V., Korniienko, V., Diedkova, K., Viter, R., and Ramanavicius, A. (2023). Towards electrochemical sensor based on molecularly imprinted polypyrrole for the detection of bacteria—*Listeria monocytogenes*. Polymers *15*, 1597. https://doi.org/10.3390/polym15071597.

72. Antipchik, M., Reut, J., Ayankojo, A.G., Öpik, A., and Syritski, V. (2022). MIP-based electrochemical sensor for direct detection of hepatitis C virus via E2 envelope protein. Talanta *250*, 123737. https://doi.org/10.1016/j.talanta.2022.123737.

73. Wardani, N.I., Kangkamano, T., Wannapob, R., Kanatharana, P., Thavarungkul, P., and Limbut, W. (2023). Electrochemical sensor based on molecularly imprinted polymer cryogel and multiwalled carbon nanotubes for direct insulin detection. Talanta *254*, 124137. https://doi.org/10.1016/j.talanta.2022.124137.

74. Ensafi, A.A., Zakery, M., and Rezaei, B. (2019). An optical sensor with specific binding sites for the detection of thioridazine hydrochloride based on ZnO-QDs coated with molecularly imprinted polymer. Spectrochim. Acta Mol. Biomol. Spectrosc. *206*, 460–465. https://doi.org/10.1016/j.saa.2018.08.040.

75. Pathak, A.K., Limprapassorn, P., Kongruttanachok, N., and Viphavakit, C. (2022). Molecularly imprinted polymer-based optical sensor for isopropanol vapor. J. Sens. Actuat. Netw. *11*, 46. https://doi.org/10.3390/jsan11030046.

76. Lin, X., Wang, Y., Wang, L., Lu, Y., Li, J., Lu, D., Zhou, T., Huang, Z., Huang, J., Huang, H., et al. (2019). Interference-free and high precision biosensor based on surface enhanced Raman spectroscopy integrated with surface molecularly imprinted polymer technology for tumor biomarker detection in human blood. Biosens. Bioelectron. *143*, 111599. https://doi.org/10.1016/j.bios.2019.111599.

77. Tokonami, S., Nakadoi, Y., Nakata, H., Takami, S., Kadoma, T., Shiigi, H., and Nagaoka, T. (2014). Recognition of gram-negative and gram-positive bacteria with a functionalized conducting polymer film. Res. Chem. Intermed. *40*, 2327–2335. https://doi.org/10.1007/s11164-014-1609-6.

78. Çiçek, Ç., Yılmaz, F., Özgür, E., Yavuz, H., and Denizli, A. (2016). Molecularly imprinted quartz crystal microbalance sensor (QCM) for bilirubin detection. Chemosensors *4*, 21. https://doi.org/10.3390/chemosensors4040021.

79. Wangchareansak, T., Thitithanyanont, A., Chuakheaw, D., Gleeson, M.P., Lieberzeit, P.A., and Sangma, C. (2014). A novel approach to identify molecular binding to the influenza virus H5N1: screening using molecularly imprinted polymers (MIPs). Med. Chem. Commun. *5*, 617–621. https://doi.org/10.1039/C3MD00272A.

80. BelBruno, J.J. (2019). Molecularly imprinted polymers. Chem. Rev. *119*, 94–119. https://doi.org/10.1021/acs.chemrev.8b00171.

81. Bates, F. (2016). Design and development of molecularly imprinted polymers and imprinted sensors. 288. https://ddd.uab.cat/record/173932.

82. Rajpal, S., Mishra, P., and Bhakta, S. (2023). Chapter 16 - MIP-based commercial materials: Molecularly-imprinted polymers for commercial application: potentials and barriers. In Molecularly Imprinted Polymers (MIPs), M. Singh, ed. (Elsevier), pp. 391–415. https://doi.org/10.1016/B978-0-323-91925-8.00003-X.

83. Patents Assigned to MIP Technologies AB. https://patents.justia.com/assignee/mip-technologies-ab.

84. Semorex Inc. Patent. https://patents.justia.com/assignee/semorex-inc.

85. Dick, J.E., Hilterbrand, A.T., Boika, A., Upton, J.W., and Bard, A.J. (2015). Electrochemical detection of a single cytomegalovirus at an ultramicroelectrode and its antibody anchoring. Proc. Natl. Acad. Sci. *112*, 5303–5308. https://doi.org/10.1073/pnas.1504294112.

86. Luo, X., and Davis, J.J. (2013). Electrical biosensors and the label free detection of protein disease biomarkers. Chem. Soc. Rev. *42*, 5944–5962. https://doi.org/10.1039/C3CS60077G.

87. Duan, X., Li, Y., Rajan, N.K., Routenberg, D.A., Modis, Y., and Reed, M.A. (2012). Quantification of the affinities and kinetics of protein interactions using silicon nanowire biosensors. Nat. Nanotechnol. *7*, 401–407. https://doi.org/10.1038/NNANO.2012.82.

88. Kumar Prusty, A., and Bhand, S. (2019). Molecularly imprinted polyresorcinol based capacitive sensor for sulphanilamide detection. Electroanalysis *31*, 1797–1808. https://doi.org/10.1002/elan.201900099.

89. Yang, Q., Li, J., Wang, X., Peng, H., Xiong, H., and Chen, L. (2018). Strategies of molecular imprinting-based fluorescence sensors for chemical and biological analysis. Biosens. Bioelectron. *112*, 54–71. https://doi.org/10.1016/j.bios.2018.04.028.

90. Fang, L., Jia, M., Zhao, H., Kang, L., Shi, L., Zhou, L., and Kong, W. (2021). Molecularly imprinted polymer-based optical sensors for pesticides in foods: Recent advances and future trends. Trends Food Sci. Technol. *116*, 387–404. https://doi.org/10.1016/j.tifs.2021.07.039.

91. Ahmad, O.S., Bedwell, T.S., Esen, C., Garcia-Cruz, A., and Piletsky, S.A. (2019). Molecularly imprinted polymers in electrochemical and optical sensors. Trends Biotechnol. *37*, 294–309. https://doi.org/10.1016/j.tibtech.2018.08.009.

92. Pietrzyk, A., Suriyanarayanan, S., Kutner, W., Chitta, R., Zandler, M.E., and D'Souza, F. (2010). Molecularly imprinted polymer (MIP) based piezoelectric microgravimetry chemosensor for selective determination of adenine. Biosens. Bioelectron. *25*, 2522–2529. https://doi.org/10.1016/j.bios.2010.04.015.

93. El-Schich, Z., Zhang, Y., Feith, M., Beyer, S., Sternbæk, L., Ohlsson, L., Stollenwerk, M., and Wingren, A.G. (2020). Molecularly imprinted polymers in biological applications. Biotechniques *69*, 406–419. https://doi.org/10.2144/btn-2020-0091.

94. Selvolini, G., and Marrazza, G. (2017). MIP-based sensors: promising new tools for cancer biomarker determination. Sensors *17*, 718. https://doi.org/10.3390/s17040718.

95. Subramaniam, M., In, L.L.A., Kumar, A., Ahmed, N., and Nagoor, N.H. (2016). Cytotoxic and apoptotic effects of heat killed *Mycobacterium indicus pranii* (MIP) on various human cancer cell lines. Sci. Rep. *6*, 19833. https://doi.org/10.1038/srep19833.

96. Cui, F., Zhou, Z., and Zhou, H.S. (2020). Molecularly imprinted polymers and surface imprinted polymers based electrochemical biosensor for infectious diseases. Sensors *20*, 996. https://doi.org/10.3390/s20040996.

97. Jamalipour Soufi, G., Iravani, S., and Varma, R.S. (2021). Molecularly imprinted polymers for the detection of viruses: Challenges and opportunities. Analyst *146*, 3087–3100. https://doi.org/10.1039/D1AN00149C.

98. Pilvenyte, G., Ratautaite, V., Boguzaite, R., Ramanavicius, S., Chen, C.F., Viter, R., and Ramanavicius, A. (2023). Molecularly imprinted polymer-based electrochemical sensors for the diagnosis of infectious diseases. Biosensors *13*, 620. https://doi.org/10.3390/bios13060620.

99. Tasić, T., Milanković, V., Pašti, I.A., and Lazarević-Pašti, T. (2024). Harnessing Molecularly Imprinted Polymers as Artificial Antibodies in Electrochemical Sensors for Disease Detection and Monitoring. In Molecularly Imprinted Polymers: Path to Artificial Antibodies, S. Patra, S.K. Shukla, and M. Sillanpää, eds. (Springer Nature Singapore), pp. 201–244. https://doi.org/10.1007/978-981-97-4379-7_7.

100. Chen, J., Lei, S., Zeng, K., Wang, M., Asif, A., and Ge, X. (2017). Catalase-imprinted Fe_3O_4/Fe@ fibrous SiO_2/polydopamine nanoparticles: An integrated nanoplatform of magnetic targeting, magnetic resonance imaging, and dual-mode cancer therapy. Nano Res *10*, 2351–2363. https://doi.org/10.1007/s12274-017-1431-8.

101. Shinde, S., El-Schich, Z., Malakpour-Permlid, A., Wan, W., Dizeyi, N., Mohammadi, R., Rurack, K., Gjörloff Wingren, A., and Sellergren, B. (2015). Sialic acid-imprinted fluorescent core–shell particles for selective labeling of cell surface glycans. J. Am. Chem. Soc. *137*, 13908–13912. https://doi.org/10.1021/jacs.5b08482.

102. Vaneckova, T., Bezdekova, J., Han, G., Adam, V., and Vaculovicova, M. (2020). Application of molecularly imprinted polymers as artificial receptors for imaging. Acta Biomater. *101*, 444–458. https://doi.org/10.1016/j.actbio.2019.11.007.

103. Kunath, S., Panagiotopoulou, M., Maximilien, J., Marchyk, N., Sänger, J., and Haupt, K. (2015). Cell and tissue imaging with molecularly imprinted polymers as plastic antibody mimics. Adv. Healthc. Mater. *4*, 1322–1326. https://doi.org/10.1002/adhm.201500145.

104. Kunath, S., Marchyk, N., Haupt, K., and Feller, K.H. (2013). Multi-objective optimization and design of experiments as tools to tailor molecularly imprinted polymers specific for glucuronic acid. Talanta *105*, 211–218. https://doi.org/10.1016/j.talanta.2012.11.029.

105. Wang, J., Dai, J., Xu, Y., Dai, X., Zhang, Y., Shi, W., Sellergren, B., and Pan, G. (2019). Molecularly imprinted fluorescent test strip for direct, rapid, and visual dopamine detection in tiny amount of biofluid. Small *15*, 1803913. https://doi.org/10.1002/smll.201803913.

106. Patriarchi, T., Cho, J.R., Merten, K., Howe, M.W., Marley, A., Xiong, W.-H., Folk, R.W., Broussard, G.J., Liang, R., Jang, M.J., et al. (2018). Ultrafast neuronal imaging of dopamine dynamics with designed genetically encoded sensors. Science *360*, eaat4422. https://doi.org/10.1126/science.aat4422.

107. Lawai, V., Ngaini, Z., Farooq, S., Wahi, R., and Bhawani, S.A. (2024). Current advances in molecularly imprinted polymers and their release mechanisms in drug delivery systems. Polym. Adv. Technol. *35*, e6317. https://doi.org/10.1002/pat.6317.

108. Liu, R., and Poma, A. (2021). Advances in molecularly imprinted polymers as drug delivery systems. Molecules *26*, 3589. https://doi.org/10.3390/molecules26123589.

109. Bărăian, A.I., Iacob, B.C., Bodoki, A.E., and Bodoki, E. (2022). In vivo applications of molecularly imprinted polymers for drug delivery: A pharmaceutical perspective. Int. J. Mol. Sci. *23*, 14071. https://doi.org/10.3390/ijms232214071.

110. Kupai, J., Razali, M., Buyuktiryaki, S., Kecili, R., and Szekely, G. (2017). Long-term stability and reusability of molecularly imprinted polymers. Polym. Chem. *8*, 666–673. https://doi.org/10.1039/C6PY01853J.

111. Erdem, Ö., Eş, I., Saylan, Y., Atabay, M., Gungen, M.A., Ölmez, K., Denizli, A., and Inci, F. (2023). In situ synthesis and dynamic simulation of molecularly imprinted polymeric nanoparticles on a micro-reactor system. Nat. Commun. *14*, 4840. https://doi.org/10.1038/s41467-023-40413-8.

112. Kandi, M.T.S., Meshkat, S.S., Hosseinzadeh, S., and Behroozsarand, A. (2023). Synthesis & characterization of novel MIP with RAFT polymerization of (2-hydroxy ethyl methacrylate)/chitosan as a nanocarrier for drug delivery applications. Int. J. Biol. Macromol. *250*, 126052. https://doi.org/10.1016/j.ijbiomac.2023.126052.

113. Zaidi, S.A. (2016). Molecular imprinted polymers as drug delivery vehicles. Drug Deliv. *23*, 2262–2271. https://doi.org/10.3109/10717544.2014.970297.

114. Wei, Z., Mu, L., and Liu, Z. (2021). In MIP as Drug Delivery Systems for Dermal Delivery BT - Molecularly Imprinted Polymers as Advanced Drug Delivery Systems: Synthesis, Character and Application, Z. Liu, Y. Huang, and Y. Yang, eds. (Springer Singapore), pp. 111–131. https://doi.org/10.1007/978-981-16-0227-6_6.

115. Ruela, A.L.M., Figueiredo, E.C., and Pereira, G.R. (2014). Molecularly imprinted polymers as nicotine transdermal delivery systems. Chem. Eng. J. *248*, 1–8. https://doi.org/10.1016/j.cej.2013.12.106.

116. Ruela, A.L.M., de Figueiredo, E.C., Carvalho, F.C., de Araújo, M.B., and Pereira, G.R. (2018). Adsorption and release of nicotine from imprinted particles synthesised by precipitation polymerisation: Optimising transdermal formulations. Eur. Polym. J. *100*, 67–76. https://doi.org/10.1016/j.eurpolymj.2018.01.021.

117. Suedee, R., Srichana, T., and Martin, G.P. (2000). Evaluation of matrices containing molecularly imprinted polymers in the enantioselective-controlled delivery of β-blockers. J. Control. Release *66*, 135–147. https://doi.org/10.1016/S0168-3659(99)00261-8.

118. Bodhibukkana, C., Srichana, T., Kaewnopparat, S., Tangthong, N., Bouking, P., Martin, G.P., and Suedee, R. (2006). Composite membrane of bacterially-derived cellulose and molecularly imprinted polymer for use as a transdermal enantioselective controlled-release system of racemic propranolol. J. Control. Release *113*, 43–56. https://doi.org/10.1016/j.jconrel.2006.03.007.

119. Jantarat, C., Tangthong, N., Songkro, S., Martin, G.P., and Suedee, R. (2008). S-Propranolol imprinted polymer nanoparticle-on-microsphere composite porous cellulose membrane for the enantioselectively controlled delivery of racemic propranolol. Int. J. Pharm. *349*, 212–225. https://doi.org/10.1016/j.ijpharm.2007.07.030.

120. Hoti, G., Ferrero, R., Caldera, F., Trotta, F., Corno, M., Pantaleone, S., Desoky, M.M.H., and Brunella, V. (2023). A comparison between the molecularly imprinted and non-molecularly imprinted cyclodextrin-based nanosponges for the transdermal delivery of melatonin. Polymers *15*, 1543. https://doi.org/10.3390/polym15061543.

121. Sreenivasan, K. (1999). On the application of molecularly imprinted poly(HEMA) as a template responsive release system. J. Appl. Polym. Sci. *71*, 1819–1821. https://doi.org/10.1002/(SICI)1097-4628(19990314)71:11<1819::AID-APP11>3.0.CO;2-E.

122. Omranipour, H.M., Sajadi Tabassi, S.A., Kowsari, R., Rad, M.S., and Mohajeri, S.A. (2015). Brimonidine imprinted hydrogels and evaluation of their binding and releasing properties as new ocular drug delivery systems. Curr. Drug Deliv. *12*, 717–725. https://doi.org/10.2174/1567201812666150316110838.

123. Raesian, P., Rad, M.S., Khodaverdi, E., Motamedshariaty, V.S., and Mohajeri, S.A. (2021). Preparation and characterization of fluorometholone molecular imprinted soft contact lenses as ocular controlled drug delivery systems. J. Drug Deliv. Sci. Technol. *64*, 102591. https://doi.org/10.1016/j.jddst.2021.102591.

124. Moradi Falah Langeroodi, S., Kazemipour, M., Eslaminejad, T., Naghipour, A., and Ansari, M. (2022). Molecular imprinted polymer with dorzolamide for contact lens applications assisted by computational and experimental design. React. Funct. Polym. *178*, 105355. https://doi.org/10.1016/j.reactfunctpolym.2022.105355.

125. Malakooti, N., Alexander, C., and Alvarez-Lorenzo, C. (2015). Imprinted contact lenses for sustained release of polymyxin B and related antimicrobial peptides. J. Pharm. Sci. *104*, 3386–3394. https://doi.org/10.1002/jps.24537.

126. Varela-Garcia, A., Gomez-Amoza, J.L., Concheiro, A., and Alvarez-Lorenzo, C. (2020). Imprinted contact lenses for ocular administration of antiviral drugs. Polymers *12*, 2026. https://doi.org/10.3390/polym12092026.

127. Liu, H., Deng, Z., Bu, J., Zhang, Y., Zhang, Z., He, Y., Li, T., Gao, P., Yang, Y., and Zhong, S. (2021). Capsule-like molecular imprinted polymer nanoparticles for targeted and chemophotothermal synergistic cancer therapy. Colloids Surf. B Biointerfaces *208*, 112126. https://doi.org/10.1016/j.colsurfb.2021.112126.

128. Gagliardi, M. (2023). Design and development of molecularly imprinted biodegradable polymers for nanomedicine. Adv. Ind. Eng. Polym. Res. *6*, 396–406. https://doi.org/10.1016/j.aiepr.2023.04.002.

129. Li, J., Wang, Q., Xia, G., Adilijiang, N., Li, Y., Hou, Z., Fan, Z., and Li, J. (2023). Recent advances in targeted drug delivery strategy for enhancing oncotherapy. Pharmaceutics *15*, 2233. https://doi.org/10.3390/pharmaceutics15092233.

130. Topçu, A.A., Kılıç, S., Özgür, E., Türkmen, D., and Denizli, A. (2022). Inspirations of biomimetic affinity ligands: A review. ACS Omega *7*, 32897–32907. https://doi.org/10.1021/acsomega.2c03530.

131. Asadi, E., Abdouss, M., Leblanc, R.M., Ezzati, N., Wilson, J.N., and Kordestani, D. (2016). Synthesis, characterization and in vivo drug delivery study of a biodegradable nano-structured molecularly imprinted polymer based on cross-linker of fructose. Polymer *97*, 226–237. https://doi.org/10.1016/j.polymer.2016.05.031.

132. Sanadgol, N., and Wackerlig, J. (2020). Developments of Smart Drug-Delivery Systems Based on Magnetic Molecularly Imprinted Polymers for Targeted Cancer Therapy: A Short Review. Pharmaceutics *12*, 831. https://doi.org/10.3390/pharmaceutics12090831.

133. Ekpenyong-Akiba, A.E., Canfarotta, F., Abd H, B., Poblocka, M., Casulleras, M., Castilla-Vallmanya, L., Kocsis-Fodor, G., Kelly, M.E., Janus, J., Althubiti, M., et al. (2019). Detecting and targeting senescent cells using molecularly imprinted nanoparticles. Nanoscale Horiz. *4*, 757–768. https://doi.org/10.1039/C8NH00473K.

134. Zhang, Y., Deng, C., Liu, S., Wu, J., Chen, Z., Li, C., and Lu, W. (2015). Active targeting of tumors through conformational epitope imprinting. Angew. Chem. Int. Ed. Engl. *54*, 5157–5160. https://doi.org/10.1002/anie.201412114.

135. Yuksel, N., and Tektas, S. (2022). Molecularly imprinted polymers: preparation, characterisation, and application in drug delivery systems. J. Microencapsul. *39*, 176–196. https://doi.org/10.1080/02652048.2022.2055185.

136. Yin, Y., Guan, L., Wang, Y., Ma, Y., Pan, J., Peng, Y., and Pan, G. (2021). Sialic acid-imprinted mesoporous nanocarriers for tumor cell targeted drug delivery. Colloid Interf. Sci. Commun. *42*, 100421. https://doi.org/10.1016/j.colcom.2021.100421.

137. Lu, H., Xu, S., Guo, Z., Zhao, M., and Liu, Z. (2021). Redox-responsive molecularly imprinted nanoparticles for targeted intracellular delivery of

protein toward cancer therapy. ACS Nano *15*, 18214–18225. https://doi.org/10.1021/acsnano.1c07166.

138. Canfarotta, F., Lezina, L., Guerreiro, A., Czulak, J., Petukhov, A., Daks, A., Smolinska-Kempisty, K., Poma, A., Piletsky, S., and Barlev, N.A. (2018). Specific drug delivery to cancer cells with double-imprinted nanoparticles against epidermal growth factor receptor. Nano Lett. *18*, 4641–4646. https://doi.org/10.1021/acs.nanolett.7b03206.

139. Hashemi-Moghaddam, H., Zavareh, S., Karimpour, S., and Madanchi, H. (2017). Evaluation of molecularly imprinted polymer based on HER2 epitope for targeted drug delivery in ovarian cancer mouse model. React. Funct. Polym. *121*, 82–90. https://doi.org/10.1016/j.reactfunctpolym.2017.10.025.

140. Suksuwan, A., Lomlim, L., Rungrotmongkol, T., Nakpheng, T., Dickert, F.L., and Suedee, R. (2015). The composite nanomaterials containing (R)-thalidomide-molecularly imprinted polymers as a recognition system for enantioselective- controlled release and targeted drug delivery. J. Appl. Polym. Sci., 132. https://doi.org/10.1002/app.41930.

141. Bărăian, A.-I., Iacob, B.-C., Soriţău, O., Tomuţă, I., Tefas, L.R., Barbu-Tudoran, L., Şuşman, S., and Bodoki, E. (2023). Ruxolitinib-loaded imprinted polymeric drug reservoir for the local management of post-surgical residual glioblastoma cells. Polymers *15*, 965. https://doi.org/10.3390/polym15040965.

142. Guo, Z., Xu, W., Xu, G., and Jia, Q. (2023). An updated overview of MOF@MIP in drug carrier and drug analysis: Construction, application and prospective. TrAC Trends Anal. Chem. *167*, 117275. https://doi.org/10.1016/j.trac.2023.117275.

143. Qin, Y.T., Feng, Y.S., Ma, Y.J., He, X.W., Li, W.Y., and Zhang, Y.K. (2020). Tumor-sensitive biodegradable nanoparticles of molecularly imprinted polymer-stabilized fluorescent zeolitic imidazolate framework-8 for targeted imaging and drug delivery. ACS Appl. Mater. Interfaces *12*, 24585–24598. https://doi.org/10.1021/acsami.0c05154.

144. Song, Y., Han, S., Liu, S., Sun, R., Zhao, L., and Yan, C. (2023). Biodegradable Imprinted Polymer Based on ZIF-8/DOX-HA for Synergistically Targeting Prostate Cancer Cells and Controlled Drug Release with Multiple Responses. ACS Appl. Mater. Interfaces *15*, 25339–25353. https://doi.org/10.1021/acsami.3c02647.

145. Han, S., Song, Y., Liu, S., Zhao, L., and Sun, R. (2022). Dual responsive molecularly imprinted polymers based on UiO-66-DOX for selective targeting tumor cells and controlled drug release. Eur. Polym. J. *171*, 111219. https://doi.org/10.1016/j.eurpolymj.2022.111219.

146. Peng, H., Qin, Y.T., He, X.W., Li, W.Y., and Zhang, Y.K. (2020). Epitope molecularly imprinted polymer nanoparticles for chemo-/photodynamic synergistic cancer therapy guided by targeted fluorescence imaging. ACS Appl. Mater. Interfaces *12*, 13360–13370. https://doi.org/10.1021/acsami.0c00468.

147. Medina Rangel, P.X., Moroni, E., Merlier, F., Gheber, L.A., Vago, R., Tse Sum Bui, B., and Haupt, K. (2020). Chemical antibody mimics inhibit cadherin-mediated cell–cell adhesion: A promising strategy for cancer therapy. Angew. Chem. Int. Ed. Engl. *59*, 2816–2822. https://doi.org/10.1002/anie.201910373.

148. Wen, M., Shi, H., Wan, Y., Wu, J., Tian, X., Chen, Q., Wu, M.-Y., and Feng, S. (2023). A human VEGF magnetic molecularly imprinted polymer for drug-free anti-angiogenesis and photothermal therapy of tumors. Chem. Commun. *59*, 4229–4232. https://doi.org/10.1039/D3CC00088E.

149. Dong, Y., Li, W., Gu, Z., Xing, R., Ma, Y., Zhang, Q., and Liu, Z. (2019). Inhibition of HER2-positive breast cancer growth by blocking the HER2 signaling pathway with HER2-glycan-imprinted nanoparticles. Angew. Chem. Int. Ed. Engl. *58*, 10621–10625. https://doi.org/10.1002/anie.201904860.

150. Feng, Y.S., Qin, Y.T., Zhuang, J., Ma, Y.J., He, X.W., Li, W.Y., and Zhang, Y.K. (2023). Mitochondria-targeted thymidylate synthase inhibitor based on fluorescent molecularly imprinted polymers for tumor antimetabolic therapy. ACS Appl. Mater. Interfaces *15*, 31139–31149. https://doi.org/10.1021/acsami.3c02883.

151. Mao, C., Xie, X., Liu, X., Cui, Z., Yang, X., Yeung, K.W.K., Pan, H., Chu, P.K., and Wu, S. (2017). The controlled drug release by pH-sensitive molecularly imprinted nanospheres for enhanced antibacterial activity. Mater. Sci. Eng. C *77*, 84–91. https://doi.org/10.1016/j.msec.2017.03.259.

152. Khademi, R., and Kharaziha, M. (2024). Antibacterial and osteogenic doxycycline imprinted bioglass microspheres to combat bone infection. ACS Appl. Mater. Interfaces *16*, 31966–31982. https://doi.org/10.1021/acsami.4c03501.

153. Elhabal, S.F., Abdelmonem, R., El Nashar, R.M., Elrefai, M.F.M., Hamdan, A.M.E., Safwat, N.A., Shoela, M.S., Hassan, F.E., Rizk, A., Kabil, S.L., et al. (2024). Enhanced antibacterial activity of clindamycin using molecularly imprinted polymer nanoparticles loaded with polyurethane nanofibrous scaffolds for the treatment of acne vulgaris. Pharmaceutics *16*, 947. https://doi.org/10.3390/pharmaceutics16070947.

154. Zhang, L.P., Tan, X.X., Huang, Y.P., and Liu, Z.S. (2018). Floating liquid crystalline molecularly imprinted polymer coated carbon nanotubes for levofloxacin delivery. Eur. J. Pharm. Biopharm. *127*, 150–158. https://doi.org/10.1016/j.ejpb.2018.02.012.

155. Liu, X.L., Yao, H.F., Chai, M.H., He, W., Huang, Y.P., and Liu, Z.S. (2018). Green synthesis of carbon nanotubes-reinforced molecularly imprinted polymer composites for drug delivery of fenbufen. AAPS PharmSciTech *19*, 3895–3906. https://doi.org/10.1208/s12249-018-1192-z.

156. Puoci, F. (2020). "Monoclonal-type" plastic antibodies for COVID-19 treatment: What is the idea? J. Funct. Biomater. *11*, 43. https://doi.org/10.3390/jfb11020043.

157. Rostamizadeh, K., Vahedpour, M., and Bozorgi, S. (2012). Synthesis, characterization and evaluation of computationally designed nanoparticles of molecular imprinted polymers as drug delivery systems. Int. J. Pharm. *424*, 67–75. https://doi.org/10.1016/j.ijpharm.2011.12.054.

158. Liu, Z., Ma, X., Li, S., Qiu, J., Liu, S., Huang, Z., Lin, H., and Abd El-Aty, A.M. (2023). Development of a biocompatible green drug release system using salidroside-TiO_2-doped chitosan oligosaccharide molecularly imprinted polymers. Arab. J. Chem. *16*, 105130. https://doi.org/10.1016/j.arabjc.2023.105130.

159. Tadi, K.K., Divakarla, P.S., and Motghare, R.V. (2013). Synthesis and characterization of pindolol imprinted polymer. Trans. Indian Inst. Met. *66*, 349–352. https://doi.org/10.1007/s12666-013-0273-7.

160. Yu, Z., Xu, Z., Li, H., Chen, J., Huang, Z., and Tang, Y. (2014). Recognition and neutralization of angiotensins I and II using an artificial nanogel receptor fabricated by ligand specificity determinant imprinting. Chem. Commun. *50*, 2728–2731. https://doi.org/10.1039/C3CC48152B.

161. Costa, R.C., Nagay, B.E., Villa, J.E.L., Sotomayor, M.D.P.T., Neres, L.C. da S., Benso, B., Aguayo, S., Sacramento, C.M., Ruiz, K.G.S., Spada, F.P., et al. (2024). Pathogenesis-guided engineering: pH-responsive imprinted polymer co-delivering folate for inflammation-resolving as immunotherapy in implant-related infections. Adv. Funct. Mater. *34*, 2406640. https://doi.org/10.1002/adfm.202406640.

162. Soliman, M., Shanan, N., Eissa, G., Mizaikoff, B., and El Gohary, N.A. (2023). In vivo application of magnetic molecularly imprinted polymer in rheumatoid arthritis rat model. J. Drug Target. *31*, 878–888. https://doi.org/10.1080/1061186X.2023.2247584.

163. Zhong, L., Zhai, J., Ma, Y., Huang, Y., Peng, Y., Wang, Y.E., Peng, Z., Gan, H., Yuan, Z., Yan, P., et al. (2022). Molecularly imprinted polymers with enzymatic properties reduce cytokine release syndrome. ACS Nano *16*, 3797–3807. https://doi.org/10.1021/acsnano.1c08297.

164. Ruela, A.L.M., de Figueiredo, E.C., de Araújo, M.B., Carvalho, F.C., and Pereira, G.R. (2016). Molecularly imprinted microparticles in lipid-based formulations for sustained release of donepezil. Eur. J. Pharm. Sci. *93*, 114–122. https://doi.org/10.1016/j.ejps.2016.08.019.

165. Torabi, S.J., Mohebali, A., Abdouss, M., Shakiba, M., Abdouss, H., Ramakrishna, S., Teo, Y.S., Jafari, I., and Rezvani Ghomi, E. (2021). Synthesis and characterization of a novel molecularly imprinted polymer for the

controlled release of rivastigmine tartrate. Mater. Sci. Eng. C *128*, 112273. https://doi.org/10.1016/j.msec.2021.112273.

166. Balcer, E., Sobiech, M., and Luliński, P. (2023). Molecularly imprinted carriers for diagnostics and therapy—A critical appraisal. Pharmaceutics *15*, 1647. https://doi.org/10.3390/pharmaceutics15061647.
167. Siddique, S., and Chow, J.C.L. (2022). Recent advances in functionalized nanoparticles in cancer theranostics. Nanomaterials *12*, 2826. https://doi.org/10.3390/nano12162826.
168. Cabaleiro-Lago, C., Hasterok, S., Gjörloff Wingren, A., and Tassidis, H. (2023). Recent advances in molecularly imprinted polymers and their disease-related applications. Polymers *15*, 4199. https://doi.org/10.3390/polym15214199.
169. Kojima, R., Aubel, D., and Fussenegger, M. (2015). Novel theranostic agents for next-generation personalized medicine: small molecules, nanoparticles, and engineered mammalian cells. Curr. Opin. Chem. Biol. *28*, 29–38. https://doi.org/10.1016/j.cbpa.2015.05.021.
170. Wang, H.-Y., Su, Z.-C., He, X.-W., Li, W.-Y., and Zhang, Y.-K. (2021). H_2O_2self-supplying degradable epitope imprinted polymers for targeted fluorescence imaging and chemodynamic therapy. Nanoscale *13*, 12553–12564. https://doi.org/10.1039/D1NR02524D.
171. Ferrari, S.M., Centanni, M., Virili, C., Miccoli, M., Ferrari, P., Ruffilli, I., Ragusa, F., Antonelli, A., and Fallahi, P. (2019). Sunitinib in the treatment of thyroid cancer. Curr. Med. Chem. *26*, 963–972. https://doi.org/10.2174/0929867324666171006165942.
172. Parisi, O.I., Ruffo, M., Malivindi, R., Vattimo, A.F., Pezzi, V., and Puoci, F. (2020). Molecularly imprinted polymers (MIPs) as theranostic systems for sunitinib controlled release and self-monitoring in cancer therapy. Pharmaceutics *12*, 41. https://doi.org/10.3390/pharmaceutics12010041.
173. Wang, H.Y., Cao, P.P., He, Z.Y., He, X.W., Li, W.Y., Li, Y.H., and Zhang, Y.K. (2019). Targeted imaging and targeted therapy of breast cancer cells via fluorescent double template-imprinted polymer coated silicon nanoparticles by an epitope approach. Nanoscale *11*, 17018–17030. https://doi.org/10.1039/C9NR04655K.
174. Saylan, Y., Akgönüllü, S., Yavuz, H., Ünal, S., and Denizli, A. (2019). Molecularly imprinted polymer based sensors for medical applications. Sensors *19*, 1279. https://doi.org/10.3390/s19061279.
175. Setia, A., Mehata, A.K., Priya, V., Pawde, D.M., Jain, D., Mahto, S.K., and Muthu, M.S. (2023). Current advances in nanotheranostics for molecular imaging and therapy of cardiovascular disorders. Mol. Pharm. *20*, 4922–4941. https://doi.org/10.1021/acs.molpharmaceut.3c00582.
176. Alagarsamy, K.N., Mathan, S., Yan, W., Rafieerad, A., Sekaran, S., Manego, H., and Dhingra, S. (2021). Carbon nanomaterials for cardiovascular theranostics: Promises and challenges. Bioact. Mater. *6*, 2261–2280. https://doi.org/10.1016/j.bioactmat.2020.12.030.
177. Liu, Y., Li, C., Yang, X., Yang, B., and Fu, Q. (2024). Stimuli-responsive polymer-based nanosystems for cardiovascular disease theranostics. Biomater. Sci. *12*, 3805–3825. https://doi.org/10.1039/D4BM00415A.
178. Fu, Q., Yu, L., Wang, Y., Li, P., and Song, J. (2023). Biomarker-responsive nanosystems for chronic disease theranostics. Adv. Funct. Mater. *33*, 2206300. https://doi.org/10.1002/adfm.202206300.
179. Sharma, D., and Singh, J. (2020). Long-term glycemic control and prevention of diabetes complications in vivo using oleic acid-grafted-chitosan-zinc-insulin complexes incorporated in thermosensitive copolymer. J. Control. Release *323*, 161–178. https://doi.org/10.1016/j.jconrel.2020.04.012.
180. Saï, P., Damgé, C., Rivereau, A.S., Hoeltzel, A., and Gouin, E. (1996). Prophylactic oral administration of metabolically active insulin entrapped in isobutylcyanoacrylate nanocapsules reduces the incidence of diabetes in nonobese diabetic mice. J. Autoimmun. *9*, 713–721. https://doi.org/10.1006/jaut.1996.0093.
181. Narjinary, M., Rana, P., Sen, A., and Pal, M. (2017). Enhanced and selective acetone sensing properties of SnO_2-MWCNT nanocomposites: Promising materials for diabetes sensor. Mater. Des. *115*, 158–164. https://doi.org/10.1016/j.matdes.2016.11.042.
182. Barani, M., Sargazi, S., Mohammadzadeh, V., Rahdar, A., Pandey, S., Jha, N.K., Gupta, P.K., and Thakur, V.K. (2021). Theranostic advances of bionanomaterials against gestational diabetes mellitus: a preliminary review. J. Funct. Biomater. *12*, 54. https://doi.org/10.3390/jfb12040054.
183. Ramanathan, S., Archunan, G., Sivakumar, M., Tamil Selvan, S., Fred, A.L., Kumar, S., Gulyás, B., and Padmanabhan, P. (2018). Theranostic applications of nanoparticles in neurodegenerative disorders. Int. J. Nanomedicine *13*, 5561–5576. https://doi.org/10.2147/IJN.S149022.
184. Jiang, L., Ding, L., and Liu, G. (2023). Nanoparticle formulations for therapeutic delivery, pathogen imaging and theranostic applications in bacterial infections. Theranostics *13*, 1545–1570. https://doi.org/10.7150/thno.82790.
185. Huang, R., Hu, Q., Ko, C.N., Tang, F.K., Xuan, S., Wong, H.M., Jin, L., Li, X., and Leung, K.C.F. (2024). Nano-based theranostic approaches for infection control: current status and perspectives. Mater. Chem. Front. *8*, 9–40. https://doi.org/10.1039/D3QM01048A.
186. Verheyen, E., Schillemans, J.P., van Wijk, M., Demeniex, M.A., Hennink, W.E., and van Nostrum, C.F. (2011). Challenges for the effective molecular imprinting of proteins. Biomaterials *32*, 3008–3020. https://doi.org/10.1016/j.biomaterials.2011.01.007.
187. Lowdon, J.W., Diliën, H., Singla, P., Peeters, M., Cleij, T.J., van Grinsven, B., and Eersels, K. (2020). MIPs for commercial application in low-cost sensors and assays–An overview of the current status quo. Sens. Actuators B Chem. *325*, 128973. https://doi.org/10.1016/j.snb.2020.128973.
188. Kadhem, A.J., Gentile, G.J., and Fidalgo de Cortalezzi, M.M. (2021). Molecularly imprinted polymers (MIPs) in sensors for environmental and biomedical applications: A review. Molecules *26*, 6233. https://doi.org/10.3390/molecules26206233.
189. Vasapollo, G., Sole, R.D., Mergola, L., Lazzoi, M.R., Scardino, A., Scorrano, S., and Mele, G. (2011). Molecularly imprinted polymers: Present and future prospective. Int. J. Mol. Sci. *12*, 5908–5945. https://doi.org/10.3390/ijms12095908.
190. Hasanah, A.N., and Susanti, I. (2023). Molecularly imprinted polymers for pharmaceutical impurities: Design and synthesis methods. Polymers *15*, 3401. https://doi.org/10.3390/polym15163401.
191. Boujday, S., Méthivier, C., Beccard, B., and Pradier, C.M. (2009). Innovative surface characterization techniques applied to immunosensor elaboration and test: comparing the efficiency of Fourier transform-surface plasmon resonance, quartz crystal microbalance with dissipation measurements, and polarization modulation-reflection absorption infrared spectroscopy. Anal. Biochem. *387*, 194–201. https://doi.org/10.1016/j.ab.2009.01.031.
192. Prabakaran, K., Jandas, P.J., Luo, J., Fu, C., and Wei, Q. (2021). Molecularly imprinted poly(methacrylic acid) based QCM biosensor for selective determination of L-tryptophan. Colloids Surfaces A Physicochem. Eng. Asp. *611*, 125859. https://doi.org/10.1016/j.colsurfa.2020.125859.
193. Gkika, D.A., Tolkou, A.K., Lambropoulou, D.A., Bikiaris, D.N., Kokkinos, P., Kalavrouziotis, I.K., and Kyzas, G.Z. (2024). Application of molecularly imprinted polymers (MIPs) as environmental separation tools. RSC Appl. Polym. *2*, 127–148. https://doi.org/10.1039/d3lp00203a.