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REVIEW

How Molecularly Imprinted Polymers can be Used for Diagnostic and Treatment of Tropical Diseases?

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Abstract
Molecularly imprinted polymers (MIPs) have been widely used in nanomedicine in the last few years. However, their use for diagnostic and treatment of tropical diseases is limited. Through this review, we aim to illustrate how MIPs were used to detect tropical disease and we show that they are not exploited enough in treatment. We finally show how MIPs could be used in the future in the treatment of tropical disease.

Keywords Molecularly imprinted polymer · Tropical disease · Treatment

1 Introduction

Over the last two decades, biodegradable polymeric materials for biomedical applications have advanced significantly [1, 2]. Biodegradable polymers have emerged as promising materials in therapeutic devices due to their biocompatibility, biodegradability, and minimal toxicity and they have been used for controlled/sustained drug release. As a result, natural or synthetic polymers able to encapsulate drugs is being studied for biomedical applications [3, 4].

In this context, very recently molecularly imprinted polymers (MIPs) (Fig. 1) have been used to confer the in vivo targeting properties of nanoparticles [5]. MIPs are synthesized after the polymerization of a functional monomer in the presence of a molecule of interest (template) with a cross-linking agent. Then, the molecule is extracted and the polymer matrix contains tailor-made binding sites, perfectly complementary to the extracted molecule [6].

In contrast to therapeutic antibodies, the synthesis of MIPs is fast, economical and they are physically and chemically stable. Due to these remarkable properties, there is an increased interest concerning the use of MIPs in nanomedicine [7]. For example, MIPs have been employed by Cecchini et al. to target specific cells in Zebrafish embryos and by Koide et al. to inhibit in vivo the action of the human Vascular Endothelial Growth Factor [8]. Piletsky et al. developed an imprinted protein nanoparticle against Epidermal Growth Factor Receptor that can recognize cancer cells and passively deliver a drug [9].

Therapeutic antibodies that disrupt cell–cell adhesion mediated by dysregulated cadherins might be employed to treat cancer: in 2020, Haupt et al. published a solid-phase synthesis using an epitope, resulting in MIP nanoparticles able to selectively bind to cadherins [10]. The synthesized material proved more potent than commercially available antibodies to inhibit cell–cell adhesion and invasion of cancer.

Another potential new application of MIPs that has attracted considerable attention is drug-controlled release [11–13]. Although MIPs have not reached the clinical application yet, these materials have an enormous potential for creating satisfactory dosage forms.

However, up to now, no studies have been reported on the use of MIPs in the treatment of tropical diseases. In this review, we discuss the recent development of MIPs for medical applications related to tropical diseases and their improvement for their use in the treatment.

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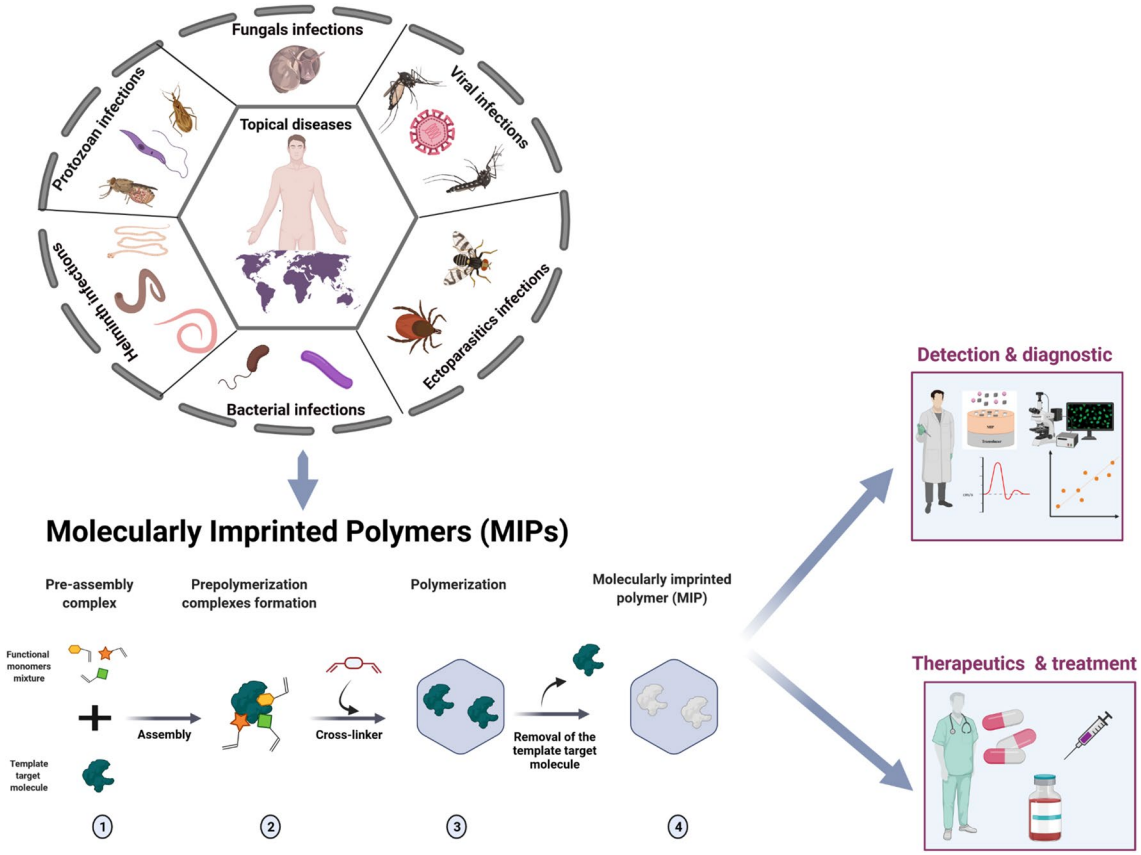

Fig. 1 Tropical diseases and MIPs. Created with BioRender.com the 3rd March 2022

2 Infectious Diseases Specific to the Tropics

Tropical infectious diseases represent a real public health problem with effects in mortality and morbidity, imposing a heavy economic burden on the affected countries which are the world's poorest populations. The available drugs for many of these diseases are not satisfactory, and for some, there are few or no treatment options at all. That's why there is a huge need for new safe, specific, inexpensive and effective treatments.

The use of MIPs could be the solution to all these challenges. However, their use for diagnostic and treatment of tropical diseases is still limited. Through this review, we aim to illustrate how MIPs were used to detect tropical disease and we show that they are not exploited enough in treatment. This review discusses some of the challenges in developing MIPs to diagnose and treat these diseases and highlights recent progress.

2.1 Tropical Diseases (Not Neglected Tropical Diseases)

Tropical diseases are those diseases that occur exclusively in countries located between the Tropic of Cancer and the Tropic of Capricorn. It includes several illnesses that occur mainly in the tropics and subtropical regions (Asia, Central and Latin America, and Africa). The main reasons that infectious diseases spread in such regions are due to environmental, biological and social factors that support high levels of biodiversity of pathogens, vectors, and hosts [14–16].

Indeed, in practice, the term is often taken to refer to all diseases, caused by nutritional deficiencies or climatic conditions (such as heat, humidity, and altitude) [17]. The climate, lack of hygiene and difficult access to health care explain the proliferation of tropical diseases in these regions. Mosquitoes or certain flies are responsible of disease transmission. These are by far the most common vectors of disease. Indeed, most often, these insects carry the infectious agent (parasite, bacterium or virus) and then transmit it by subcutaneous blood exchange to humans and animals via their "bite" [18–21]. Vaccines are not available for any of the diseases, and many do not have cures.

2.2 Neglected Tropical Diseases (NTDs)

Neglected tropical diseases (NTDs) are a diverse group of diseases that affect more than a billion people of the world's population mostly in developing countries in

tropical and subtropical areas of the world [22]. This group of diseases is intimately linked to poverty. Indeed, they thrive in areas where access to adequate sanitation, clean water and healthcare is limited, and people live in proximity with animals and infectious disease vectors, such as in remote and rural areas, informal settlements or conflict zones [23–25].

The NTDs called "neglected" are almost absent from the global health agenda. Even today, when the focus is on Universal Health Coverage, NTDs have very limited resources and are almost ignored by global funding agencies. NTDs are diseases of neglected populations that perpetuate a cycle of poor educational outcomes and limited professional opportunities.

In the early 2000s, the World Health Organization (WHO) had 17 NTDs in its portfolio, a diverse group of communicable diseases caused by a variety of pathogens including bacteria, parasites, helminths, protozoa or viruses and fungi. Since 2016, this list has been expanded with three groups of diseases to currently include 20 NTDs or groups of NTDs [26]. Those new NTDs include mycetoma, chromoblastomycosis and other deep mycoses; scabies and other ectoparasites; and snakebite envenoming (Table 1).

3 MIPs Used for the Diagnosis of Tropical Diseases

The growing interest in biosensors from a general point of view is growing by the day and represents a global market of one billion dollars. They have achieved notoriety because of their many advantages. The system is composed of bioreceptors (enzymes, genetic material, antibodies, antigens, cells or tissues) immobilized on a transducer surface that can recognize the specific analyte (Fig. 2). Antibodies are the most commonly used. However, they are expensive, lack stability and their use are limited to physiological conditions. The transducer converts the response of the biological event into a quantifiable and measurable signal.

Table 1 List of neglected tropical diseases

Pathogen	Disease
Protozoan infections 	1 Chagas disease 2 Human African trypanosomiasis 3 Leishmaniasis
Helminth infections 	4 Taenia solium / Taeniosis 5 Dracunculiasis 6 Echinococcus 7 Foodborne trematodiases 8 Lymphatic filariasis 9 Onchocerciasis 10 Schistosomiasis 11 Soil-transmitted helminthiases (ascariasis, trichuriasis)
Bacterial infections 	12 Buruli ulcer 13 Leprosy 14 Trachoma 15 Yaws
Viral infections 	16 Dengue and chikungunya fevers 17 Rabies
Fungal infections 	18 Mycetoma, chromoblastomycosis, deep mycosis
Ectoparasitic infections 	19 Scabies, Myiasis
Venom 	20 Snakebite envenoming

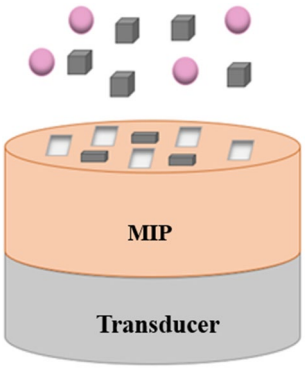

Fig. 2 General schematic representation of a MIP sensor. Created with BioRender.com the 3rd March 2022

For most tropical diseases, the best diagnostic methods are costly and time consuming. Biosensors for diagnosing NTDs are therefore of crucial importance [27].

MIP sensors are the result of several researches due to their many advantages including their high affinity and selectivity, ease of preparation or their low costs which will greatly accelerate the diagnosis and consequently the treatment [27]. These materials can be synthesized easily in any laboratory in the world, without any specific equipment. Moreover, they are very stable and not soluble, important for the development of sensors.

In the literature, many researchers are interested in MIP electrochemical biosensors for tropical diseases such as typhoid, leprosy, meningitis but also for the detection of anti-malarial drugs [28–31]. Let's take as a first example, the case of typhoid, a deadly disease if not diagnosed in time [28]. Harijan et al. have therefore been interested in the development of an epitope (protein sequence) imprinted polymer to detect the typhoid bacterium in a specific way. The epitope sequence was predicted using immunoinformatic tools and the corresponding MIP was prepared by electropolymerization. The developed sensor was verified with unpaired peptides showing remarkable selectivity of the chosen epitope. The results showed that the MIP sensor responded to infected patients and showed no response to healthy patients [28].

The epitope imprinted polymer sensor technology has been developed by other researchers to detect other tropical diseases. Kushwaha et al. looked at the mycobacterium leprae bacterium responsible for leprosy with a sensor similar to the above. The piezoelectric electrochemical MIP film sensor used to detect the epitope of the engineered mycobacterium leprae exhibits excellent detection, with high sensitivity, affinity, stability and rapid recognition of the analyte. In addition, various epitope sequences and proteins were also examined for a MIP coated film showing selective adsorption towards the epitope sequence used in its manufacture. The sensor showed good selectivity and selective recognition towards real blood samples of blood infected with mycobacterium leprae bacteria [29].

Gupta et al. paid particular attention to neisseria meningitidis, a bacterial pathogen causing bacterial meningitis. Their work aimed to propose a diagnostic tool for the detection of the bacterium using a protein imprinted polymer sensor developed on the gold surface of an electrode. The sensor specifically and selectively detects the protein associated with the epitope offering an easy and efficient diagnosis of this disease (Fig. 3) [30].

These preliminary results on epitope imprinted polymer sensors could open a new step towards reliable and cost-effective medical diagnostics for healthcare.

In recent years, biosensing methods have undergone tremendous development offering promising candidates for future diagnostics. In the literature, various bioreceptors and transducers have been used for dengue virus detection [32, 33]. The biosensor methods include amperometric, voltametric, impedimetric, potentiometric, nucleic acid-based and antibody-based biosensors [34]. Electrochemistry is one of the most sensitive and simple transduction techniques, allowing the miniaturization of devices. Arshad et al. focused on the molecularly imprinted polymer-based impedimetric sensor [34]. The screen-printed carbon electrode is modified with electrospun polysulfone nanofibers, then coated with dopamine while using NS1 (specific and sensitive biomarker of dengue virus infection) as a template during polymerization. Oxidative self-polymerization of dopamine (Fig. 4) (2-(3,4-dihydroxyphenyl)ethylamine) on surfaces is a promising method to form thin polymer films by a single deposition process while controlling the film thickness [34].

Self-polymerization at room temperature allows to maintain the exact structure of the NS1 protein and to generate geometrically adapted printed sites for the specific detection of the target analyte. The MIP sensor unsurprisingly showed excellent analytical performance in terms of sensitivity and selectivity [34]. Table 2 summarizes the different monomers used for the fabrication of the MIP sensors mentioned above.

In addition, the applicability of the proposed methods for clinical diagnosis of viruses responsible for tropical diseases have demonstrated high accuracy. The ease and low cost of these MIP sensors allow their application for the detection of other analytes in different fields.

Figure 5 shows the evolution of the number of publications related to MIP sensors (in blue) and the combination of MIP sensors for tropical diseases (in orange). It highlights that this theme is not very exploited due to the low number of publications.

It would be interesting to study this subject more closely as it could open new doors in the future concerning the diagnosis and treatment of tropical diseases.

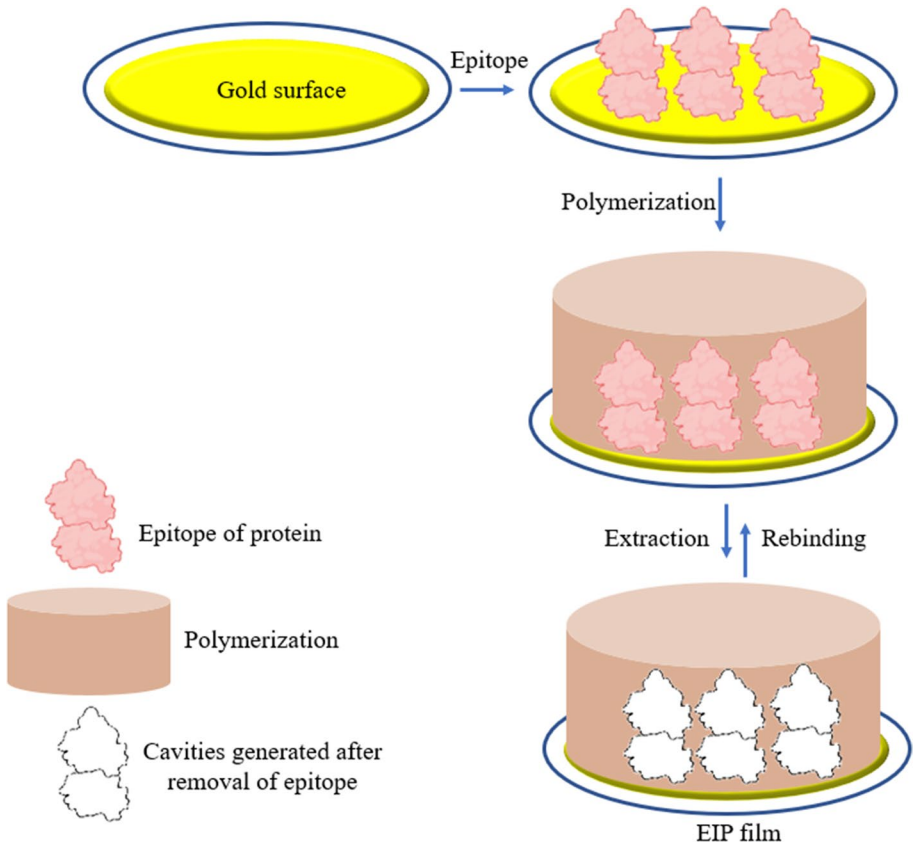

Fig. 3 Schematic representation of the preparation of the epitopic imprinted polymer coating on a quartz crystal microbalance electrode. Created with BioRender.com the 3rd March 2022

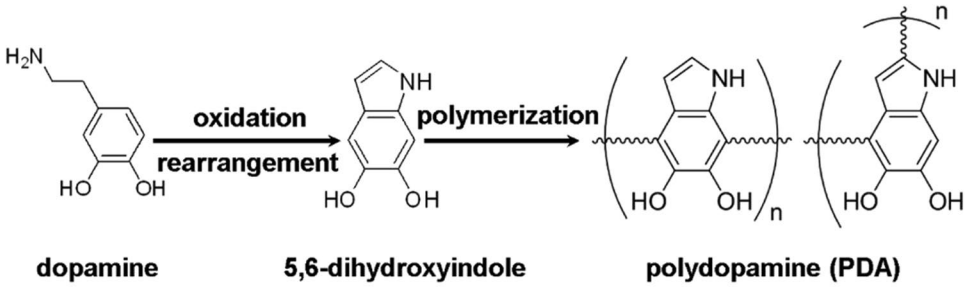

Fig. 4 Principle of dopamine self-polymerization [34]. Reproduced with permission from Springer

4 Therapeutic Applications of MIPs

4.1 Drug Delivery

The range of systems and approaches that can be used to improve drug delivery is growing and has important implications in the pharmaceutical industry. The development of new materials and technologies has reduced therapeutic side effects through enabled drug encapsulation and targeted delivery, prolonged blood circulation time and sustained or triggered drug delivery [35]. In recent years, MIP-based drug delivery systems have attracted attention because of their ability to improve loading and delivery of drugs and their stability in blood. However, only a few examples of these systems were reported for tropical disease applications (Table 3).

Zhang et al. developed the first synthesis of liquid crystalline molecularly imprinted polymers (LC-MIPs) coated multiwalled carbon nanotubes (MWCNTs) as an oral floating DDS [36]. The synthesis was achieved by functionalising MWCNTs with 9-vinylanthracene firstly, and then polymerization of LC-MIPs was performed on the surface of MWCNTs using a monomer mixture of methacrylic acid, ethylene glycol dimethacrylate, and 4-methyl phenyl dicyclohexyl ethylene (LC monomer) using levofloxacin (LVF) as a model template (Fig. 6). LVF is a broad spectrum fluoroquinolone antibiotic, used for the treatment of tuberculosis and meningitis in combination with other antibiotics [37, 38]. In vitro release experiments demonstrated that the LVF liberation

Table 2 MIPs biosensors existing for tropical diseases and how they are synthesized

Disease	Monomer(s) mixture	Sequence	Sensor type	Extraction solvent	Limit of detection	Sensitivity	Technique of characterization
Typhoid [28]	3-Sulfopropyl methacrylate potassium, Glutaraldehyde	TKIQQAQQTLQSTP	MIP-EQCM[a] sensor	PBS[b]	0.5 ng/mL	Good analytical performance	Electrochemical impedance spectroscopy Differential pulse voltammetry Protparam
Mycobacterium leprae [29]	Potassium salt of 3-sulfopropyl, Methacrylate, Benzyl methacrylate, 4-aminothiopheno, Azoisobutyronitrile	LDIYTTLARDMAAIP	MIP-EQCM[a] sensor	PBS[b]	0.161 nM	Good analytical performance	Cyclic voltammetry Electrochemical impedance spectroscopy Goniometer Atomic force microscopy
Neisseria meningitidis [30]	Methyl Methacrylate, Ethylene glycol dimethacrylate	KGLVDDADI GRHNSESYH	MIP-EQCM[a] sensor	PBS[b]	15.71 ng/mL	Good analytical performance	Piezoelectrogravimmetric measurements Atomic force microscopy Goniometer

[a]Electrochemical quartz cristal microbalance

[b]Phosphate buffered saline

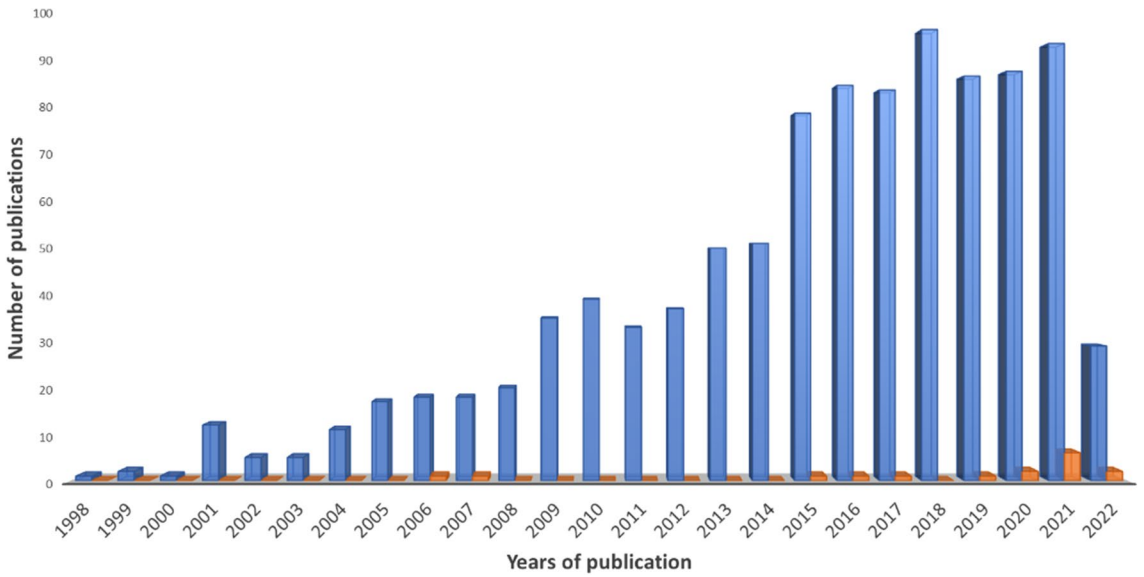

Fig. 5 Evolution of the number of publications related to MIP sensors (blue) and to the combination of MIP sensors and tropical diseases (orange). Data extracted from https://pubmed.ncbi.nlm.nih.gov/ the 3rd March 2022

from the MWCNT@LC-MIP exhibited a satisfied controlled release behavior, with a release rate of 3.8 g/h over a period of about 20 h compared to 2.6 g/h with duration of about 15 h from MWCNT@MIP. In vivo pharmacokinetic studies from Wistar rats showed that the relative bioavailability of the gastro-floating MWCNT@LC-MIP was significantly increased, compared to the MWCNT@LC-NIP. Therefore, MWCNT@LC-MIP demonstrated potential for

Table 3 MIPs synthesis used for antibiotics development

Monomer(s) mixture	Loaded antibiotics	Preparation Method	Advantages
Methacrylic acid (MAA), 4-methyl phenyl dicyclohexyl ethylene (MPDE, liquid crystalline monomer), ethylene glycol dimethacrylate (EDMA, cross linker), 2,2-azobis(2-isobutyronitrile) (AIBN, initiator)	Levofloxacin (LVF)	Thermal polymerization on the surface of multiwalled carbon nanotubes (MWCNTs)	Enhance the bioavailability of orally administered drugs [36]
Cyclodextrin (CD), epichlorohydrin (cross-linker), 1,6-diisocyanatohexane (HDI)	Rifampicin (RM), novobiocin (NB), and vancomycin (VM)	Supramolecular hydrogels	Improve drug loading without altering stability and release window of drugs [39]
2-hydroxyethyl methacrylate (HEMA), 2-(diethylamino) ethyl methacrylate (DEAEMA)	Ethylene glycol dimethacrylate (EGDMA)	UV-initiated precipitation polymerization	Improve drug release by adjusting to acidic pH to suppress bacterial infections [46]

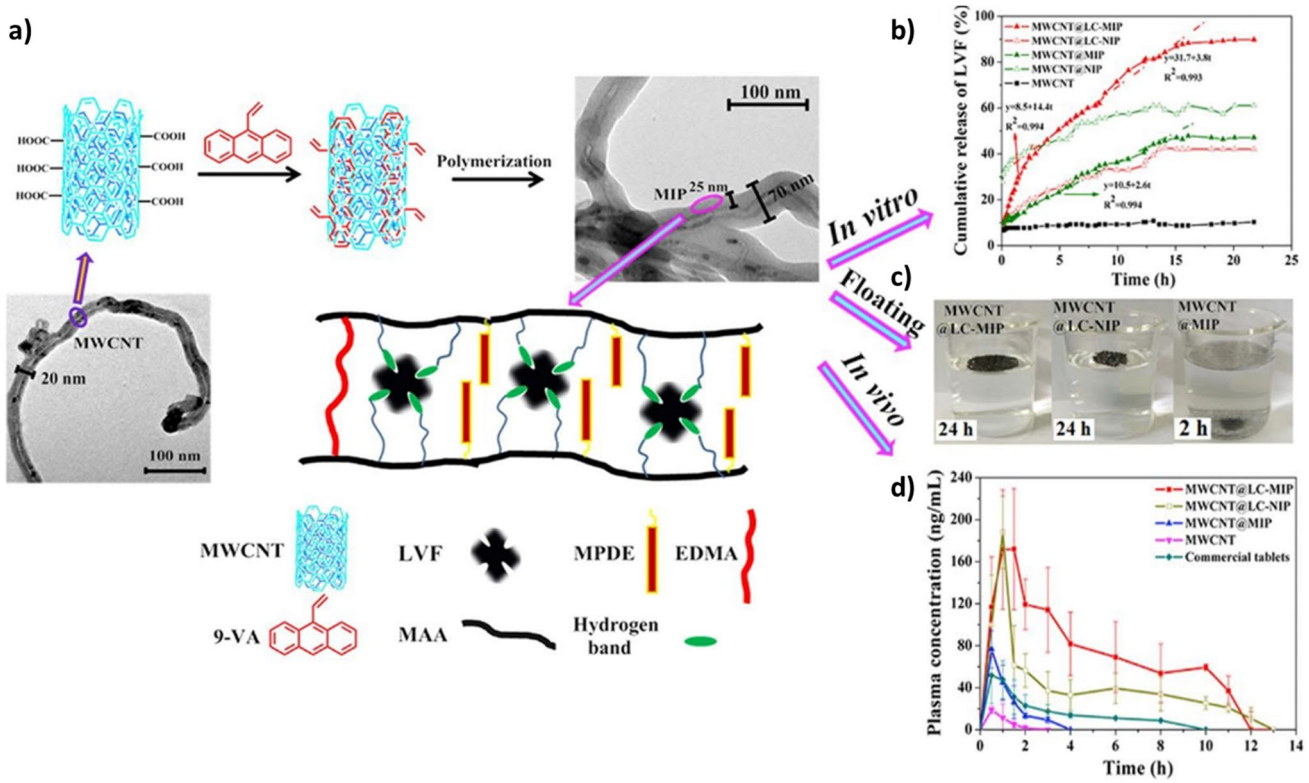

Fig. 6 The preparation of MWCNTs@LC-MIP and application in oral drug delivery of levofloxacin [36]. **a** MWCNTs@LC-MIP was successfully prepared via co-polymerization of methacrylic acid (MAA), 4-methyl phenyl dicyclohexyl ethylene (MPDE), and ethylene glycol dimethacrylate (EDMA), levofloxacin (LVF) as the template drug via surface molecular imprinting polymerization method. **b** The in vitro study suggested that the LVF had a satisfied controlled release behavior from MWCNTs@LC-MIP. **c** MWCNT@LC-MIP powders possessed the floating behavior on the aqueous medium and had significantly longer floating time (> 24 h) than the MWCNT@MIP (< 2 h) with the same mass and composition. **d** MWCNT@LC-MIP and MWCNT@LC-NIP showed enhanced bioavailability with a significantly higher value of area under the plasma concentration–time curve (AUC_{0-13}), than MWCNT@MIP, MWCNT and the commercial tablet. Reproduced with permission from ScienceDirect

oral administration by the innovative combination of floating and controlled delivery properties.

Juric and his coworkers reported the synthesis of cyclodextrin (CD) supramolecular hydrogels composed of molecularly imprinted with three antibiotics—rifampicin (RM), novobiocin (NB), and vancomycin (VA) [39]. They developed an affinity-based system that utilizes the unique properties of β-CD, a cyclic oligomer with a relatively

hydrophobic interior and a relatively hydrophilic exterior. This leads to a guest–host complex with the antibiotics through various secondary molecular interactions such as hydrogen bonding, van der Waals bonding, and hydrophobic interactions. RM is used to treat a number of bacterial infections including tuberculosis and leprosy in combination with other antibiotics [40]. They studied the influence on drug loading, release kinetics, and antimicrobial activity. Both molecularly imprinted and non-imprinted CD-based hydrogels were successfully synthesized at room temperature in order to avoid denaturing the antibiotics and therefore the templates (Fig. 7). The delivery and drug loading studies by UV–Vis spectroscopy showed an increase in total drug-loading in its respective template impressed hydrogel without altering the therapeutic release window. Finally, the bioactivity assay confirmed that long-term stability and liberation of incorporated antibiotics was not compromised by molecularly imprinted hydrogels.

Some MIPs respond to environmental stimuli and can provide more controlled drug-delivery processes [41, 42]. They have been developed with different external stimuli-responsivities including magnetic [43], pH- [44], thermo-, or/and photoresponsivity [45]. Mao et al. prepared pH-sensitive MIP nanospheres for improving antibacterial activity. They applied molecularly imprinted technology combined with a UV-initiated precipitation polymerization using vancomycin (VA) for the template (Fig. 8) [46]. VA is generally prescribed to combat severe infections caused by Staphylococcus aureus (S. aureus), it is very used for the treatment of hospital infections but also for respiratory infections, meningitis, tissue and skin infections. These MIPs exhibit a higher VA loading capacity, and a slower and long-term VA liberation than the corresponding NIPs. In addition, the MIPs were sensitive to pH values, i.e., a faster release rate and much higher release concentrations when the pH was decreased, which is desirable for suppressing bacterial infections. Furthermore, the VA-loaded MIPs demonstrated much

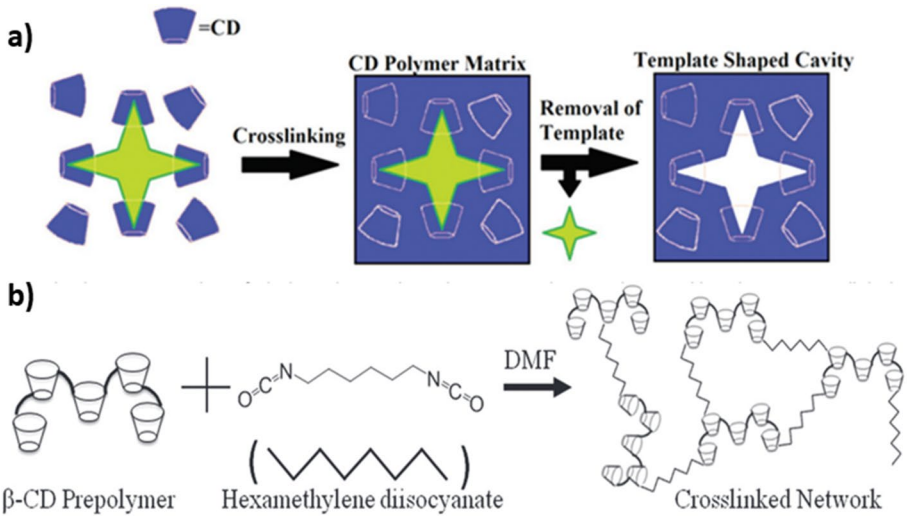

Fig. 7 The preparation of CD supramolecular hydrogels. **a** Molecular imprinting CD scheme demonstrating how templating could result in geometrically higher affinities than a linear polymer. **b** Chemical synthesis of CD-Hexamethylene diisocyanate (HDI) networks [39]. Reproduced with permission from Wiley

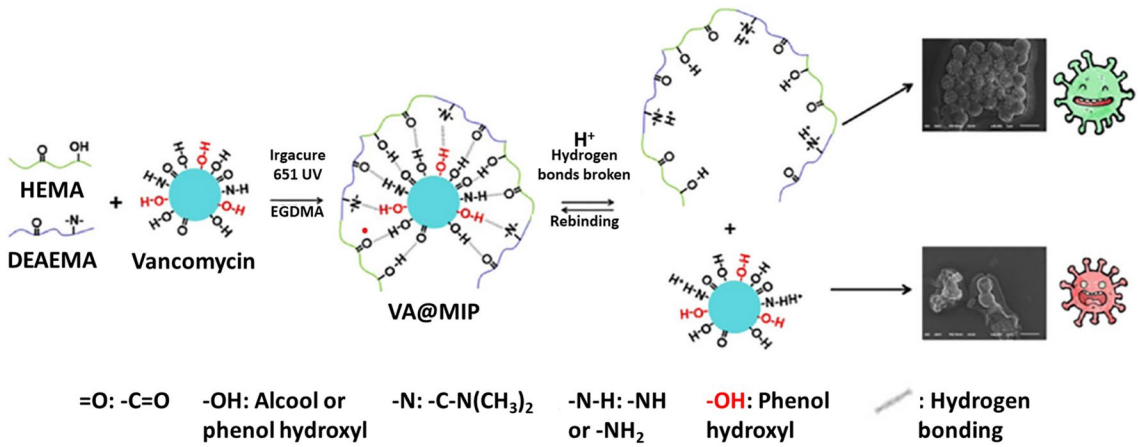

Fig. 8 Imprinting mechanism for the drug delivery system of MIPs@VA [46]. Reproduced with permission from Elsevier

higher antibacterial ratio for more than 90% to S. aureus. These results confirmed that these MIP nanospheres can be promising to achieve specific therapies such as preventing bacterial infections caused by tropical diseases.

Hence, MIPs emerge as a promising drug carrier mainly in the fields of sustained release, controlled release and targeted delivery system based on its distinct advantages. As described in this section, MIPs as drug delivery system applied to tropical diseases are still in its infancy, and more in-depth research needs to be undertaken to develop effective systems.

4.2 Biomimetic Nanomedicine

In the last few years, MIPs have been widely used for in vivo capture and neutralization of toxic substances because of their high target-recognition ability and good biocompatibility [47]. Moreover, some MIPs have been developed for their capability of strongly and selectively catching viruses, inhibiting enzymes, or sequestering proteins, which are highly promising as biomimetic nanomedicines [48, 49]. To this day, any examples in the literature have been reported related to the use of MIPs to treat a tropical viral infection, but certain existing approaches could be optimized for pathogens found in tropical areas (Table 4).

In order to respond to the ever-increasing demand for new antiviral strategies, Sankarakumar and Tong described the use of MIPs as virus catchers to prevent viral infections [50]. This work successfully demonstrates the application of miniemulsion polymerization to surface imprinting of a model virus. The particles exhibited greater virucidal action than control particles when incubated with the template virus in the absence or presence of host cells E. coli. This work can provide a new application of such imprinted materials as an ideal antiviral agent for effective virus-capture and infection inhibition in tropical disease treatment.

Although not widely studied yet, MIPs may represent promising approaches to improve the diagnosis and treatment of the current Coronavirus Disease of 2019 (COVID-2019) as well as future pandemics [51]. Parisi et al. developed "monoclonal" antibody-based MIPs for recognition and binding to a specific sequence on the SARS-CoV-2 spike protein in order to block his function [52]. Indeed, Xu et al. have found that the spike virus protein has a relevant binding affinity to human angiotensin-converting enzyme 2 (ACE2), which is the corresponding receptor on the human respiratory epithelial cells (Fig. 9). They have obtained promising preliminary results, but further studies are needed. Specifically, these MIPs showed specific and selective binding affinity and detection of the target protein by electrophoresis. They also demonstrated a good hemocompatibility, which is a key requirement for a system designed for intravenous administration. Therefore, the developed MIPs could be potentially used as free-drug therapeutics in the treatment of 2019-nCoV infection as well as tropical infections. Additionally, when loaded with antiviral agents, they could block the virus protein and be used as targeted delivery of the loaded drug.

Owing to their efficiency in biological sensors, MIPs can potentially be employed in nanomedicine. However, as a first step, comprehensive analysis of their interaction with cells and biocompatibility tests must be conducted. Canforetta et al. reported the synthesis of bare and core–shell MIPs and evaluated their toxicity in different cell lines (HaCaT, MEFs, HT1080, and macrophages) and their internalization in cells [53]. They showed that bare and coating MIP nanoparticles are biocompatible and undergo cellular internalization, which is desired for cytoplasmic drug delivery applications. Furthermore, in vitro cytokine release studies demonstrated that macrophages were not activated in the presence of the MIPs. These results suggest that MIPs have great potential for in vivo studies. For example, Hoshino et al. developed MIPs to eliminate melittin (a peptide that is the principal component of bee venom) from the bloodstream of living mice [5]. The MIPs successfully cleared melittin, improving the survival rate of the mice over 24 h and reducing the toxic

Table 4 MIPs synthesis used for virus treatment

Monomer(s) mixture	Loaded virus	Method	Method description	Applications
Methacrylate and acrylic acid, ethylene glycol dimethacrylate (EGDMA), ammonium persulfate (APS) and sodium bisulphite (initiators)	Fr bacteriophage, Fr is a small enteric phage that is specific to its bacterial host *Escherichia coli*	One-stage redox-initiated mini-emulsion polymerization	Oil phase with monomers mixture added drop-wise into an aqueous phase Reaction into a reactor maintained in a nitrogen gas atmosphere at 40 °C	Antiviral agent for effective virus-capture and infection inhibition [50]
Methacrylic acid (MAA), ethylene glycol dimethacrylate (EGDMA, cross-linker) and 2,2'-azoisobutyronitrile (AIBN, initiator)	Synthetic polymeric antibodies against SARS-CoV-2	Precipitation polymerization	Formation of a complex between the template and the functional monomers during the pre-polymerization step through non-covalent interactions	Free-drug therapeutics in the treatment of 2019-nCoV infection [52]

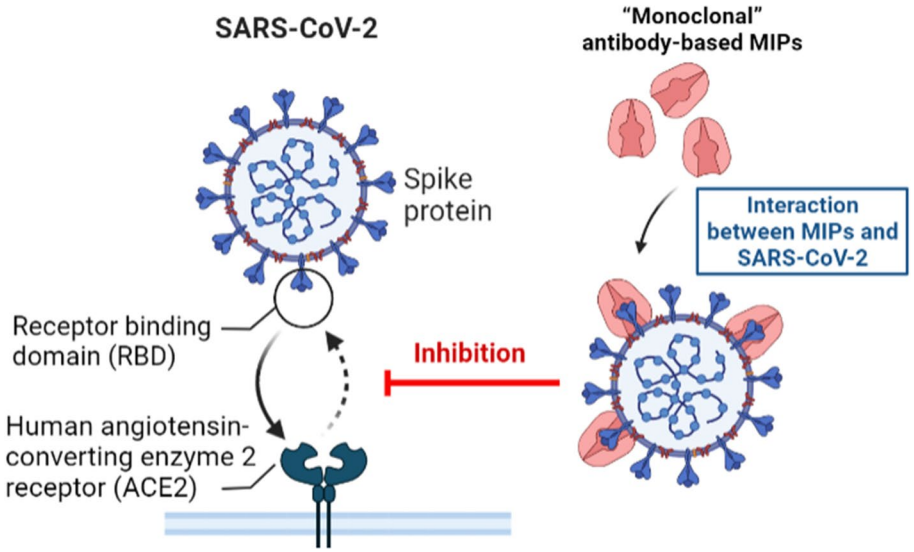

Fig. 9 Schematic representation of the interaction between "monoclonal" antibody-based MIPs and SARS-CoV-2 for the selective recognition and binding of the receptor binding domain (RBD) in order to block the function of the spike protein (Created with BioRender.com the 1st February 2022) [52]

effects of the peptide. They demonstrated the potential of MIP nanoparticles for the selective recognition of molecules in vivo. These considerations highlight the potential of MIPs for in vitro and in vivo uses, and similar studies are likely to be developed in the future years.

5 Conclusion

Molecular imprinting systems have many promising biomedical applications, especially those requiring selective binding to a target. In this review, we report the most recent applications of MIPs and how this approach can be used as a powerful tool for the diagnosis and treatment of tropical diseases. In diagnosis, MIPs represent a promising sensing element due to its capacity to recognize targeted molecules with a high affinity, its low cost and stability. They are expected to grow rapidly in medical applications. In the future, they could be used directly by the patient who could test himself without any medical assistance which will revolutionize the healthcare industry. Huge progress has been achieved in the development of sensors but there are still several challenges. The most important one is that the sensitivity and selectivity need further improvements. Hence, more functional monomers need to be probed to enhance chemical recognition. However, the use of this approach presents many challenges and remains largely unexplored in the field of tropical diseases. This review should give novel ideas to researchers interested in the detection of tropical diseases as there is still a lot to develop.

For the treatment of tropical diseases, few works, using MIPs, have been reported. As MIPs are used in nanomedicine since few years, especially in cancer treatment, its development for tropical diseases is only at an early stage. The main limitation to the use of MIPs in the treatment of tropical disease is mainly due to its biocompatibility. Hence, huge efforts should be devoted to the development of non toxic and biocompatible MIPs [53, 56]. Hybrid MIP nanoparticles have emerged as a powerful material for controlled drug delivery because they can release drug by external stimuli. We recently developed an innovative MIP nanomaterial with magnetic delivery enabling active control over drug release using AMF [43, 54, 55]. Under AMF, the magnetic nanoparticles locally heat and the hydrogen bonding between the drug and the polymer is broken and the drug is released. Based on recent works using MIP or hybrid MIP nanoparticles for controlled drug release, their use for hydroxychloroquine release to treat malaria could be a novel treatment. These innovative MIPs offer the possibility to treat tropical diseases provided that they show any toxicity and are biodegradable.

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Declarations

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References

1. Sung YK, Kim SW (2020) Recent advances in polymeric drug delivery systems. Biomater Res 24:12
2. Hans ML, Lowman AM (2002) Biodegradable nanoparticles for drug delivery and targeting. Curr Opin Solid State Mater Sci 9:319–327
3. Idrees H, Zaidi SZJ, Sabir A, Khan RU, Zhang X, Hassan S (2020) A review of biodegradable natural polymer-based nanoparticles for drug delivery applications. Nanomaterials 10:1970
4. Jana P, Shyam M, Singh S, Jayaprakash V, Dev A (2021) Biodegradable polymers in drug delivery and oral vaccination. Eur Polym J 142:110155
5. Hoshino Y, Koide H, Urakami T, Kanazawa H, Kodama T, Oku N et al (2010) Recognition, neutralization, and clearance of target peptides in the bloodstream of living mice by molecularly imprinted polymer nanoparticles: a plastic antibody. J Am Chem Soc 132:6644–6645
6. Sellergren B (2010) Shaping enzyme inhibitors. Nat Chem 2:7–8
7. Haupt K, Medina Rangel PX, Bui BTS (2020) Molecularly imprinted polymers: antibody mimics for bioimaging and therapy. Chem Rev 120:9554–9582
8. Cecchini A, Raffa V, Canfarotta F, Signore G, Piletsky S, MacDonald MP et al (2017) In vivo recognition of human vascular endothelial growth factor by molecularly imprinted polymers. Nano Lett 17:2307–2312
9. Canfarotta F, Lezina L, Guerreiro A, Czulak J, Petukhov A, Daks A et al (2018) Specific drug delivery to cancer cells with double-imprinted nanoparticles against epidermal growth factor receptor. Nano Lett 18:4641–4646
10. Medina Rangel PX, Moroni E, Merlier F, Gheber LA, Vago R, Tse Sum Bui B et al (2020) Chemical antibody mimics inhibit cadherin-mediated cell-cell adhesion: a promising strategy for cancer therapy. Angew Chem Int Ed 59:2816–2822
11. Xu Y, Hu X, Guan P, Du C, Tian Y, Ding S et al (2019) A novel controllable molecularly imprinted drug delivery system based on the photothermal effect of graphene oxide quantum dots. J Mater Sci 54:9124–9139
12. Kan X, Geng Z, Zhao Y, Wang Z, Zhu J-J (2009) Magnetic molecularly imprinted polymer for aspirin recognition and controlled release. Nanotechnology 20:165601
13. Asadi E, Abdouss M, Leblanc RM, Ezzati N, Wilson JN, Azodi-Deilami S (2016) In vitro/in vivo study of novel anticancer, biodegradable cross-linked tannic acid for fabrication of 5-fluorouracil-targeting drug delivery nano-device based on a molecular imprinted polymer. RSC Adv 6:37308–37318
14. Zumla A, Ustianowski A (2012) Tropical Diseases. Infect Dis Clin N Am 26:195–205
15. Booth M (2018) Climate change and the neglected tropical diseases. Adv Parasitol 100:39–126
16. Pujara P, Parmar M, Rupakar P, Asawa K, Patel S (2016) An INTRODUCTION to tropical disease: a review article. Int J Med Microbiol Trop Dis 2:81
17. Rupali P (2019) Introduction to tropical medicine. Infect Dis Clin N Am 33:1–15
18. Shuman EK (2011) Global climate change and infectious diseases. Int J Occup Environ Med 2(1):11–19
19. Colón-González FJ, Sewe MO, Tompkins AM, Sjödin H, Casallas A, Rocklöv J et al (2021) Projecting the risk of mosquito-borne diseases in a warmer and more populated world: a multi-model, multi-scenario intercomparison modelling study. Lancet Planet Health 5:e404–e414
20. Bartlow AW, Manore C, Xu C, Kaufeld KA, Del Valle S, Ziemann A et al (2019) Forecasting zoonotic infectious disease response to climate change: mosquito vectors and a changing environment. Vet Sci 6:40
21. Neglected tropical diseases: impact of COVID-19 and WHO's response—2021 update WEEKLY EPIDEMIOLOGICAL RECORD, NO 38, 461–468; (24 SEPTEMBER 2021).
22. Álvarez-Hernández D-A, Rivero-Zambrano L, Martínez-Juárez L-A, García-Rodríguez-Arana R (2020) Overcoming the global burden of neglected tropical diseases. Ther Adv Infect Dis 7:204993612096644
23. Engels D, Zhou X-N (2020) Neglected tropical diseases: an effective global response to local poverty-related disease priorities. Infect Dis Poverty 9:10
24. Tidman R, Abela-Ridder B, de Castañeda RR (2021) The impact of climate change on neglected tropical diseases: a systematic review. Trans R Soc Trop Med Hyg 115:147–168
25. Mitra A, Mawson A (2017) Neglected tropical diseases: epidemiology and global burden. Trop Med Infect Dis 2:36
26. WHO (2019) https://www.who.int/neglected_diseases/diseases/en/. Accessed 23 Jan 2019
27. Cordeiro TAR, de Resende MAC, dos Moraes SCS, Franco DL, Pereira AC, Ferreira LF (2021) Electrochemical biosensors for neglected tropical diseases: a review. Talanta 234:1617
28. Harijan M, Shukla V, Singh AK, Raghuwanshi R, Nath G, Singh M (2022) Design of molecularly imprinted sensor for detection of typhoid using immunoinformatics and molecular imprinting. Biosens Bioelectron X 10:100090
29. Kushwaha A, Srivastava J, Singh AK, Anand R, Raghuwanshi R, Rai T et al (2019) Epitope imprinting of *Mycobacterium leprae* bacteria via molecularly imprinted nanoparticles using multiple monomers approach. Biosens Bioelectron 145:111698
30. Gupta N, Shah K, Singh M (2016) An epitope-imprinted piezoelectric diagnostic tool for *Neisseria meningitidis* detection: epitope-imprinted diagnostic tool for meningitis detection. J Mol Recognit 29:572–579
31. Waffo AFT, Yesildag C, Caserta G, Katz S, Zebger I, Lensen MC et al (2018) Fully electrochemical MIP sensor for artemisinin. Sens Actuators B Chem 275:163–173
32. Anusha JR, Kim BC, Yu K-H, Raj CJ (2019) Electrochemical biosensing of mosquito-borne viral disease, dengue: A review. Biosens Bioelectron 142:111511
33. Buensuceso CE, Tiu BDB, Lee LP, Sabido PMG, Nuesca GM, Caldona EB et al (2022) Publisher correction to: electropolymerized-molecularly imprinted polymers (E-MIPS) as sensing elements for the detection of dengue infection. Anal Bioanal Chem 414:1457–1458
34. Arshad R, Rhouati A, Hayat A, Nawaz MH, Yameen MA, Mujahid A et al (2020) MIP-based impedimetric sensor for detecting dengue fever biomarker. Appl Biochem Biotechnol 191:1384–1394
35. Zhang H (2020) Molecularly imprinted nanoparticles for biomedical applications. Adv Mater 32:1806328
36. Zhang L-P, Tan X-X, Huang Y-P, Liu Z-S (2018) Floating liquid crystalline molecularly imprinted polymer coated carbon nanotubes for levofloxacin delivery. Eur J Pharm Biopharm 127:150–158
37. Deshpande D, Pasipanodya JG, Mpagama SG, Bendet P, Srivastava S, Koeuth T et al (2018) Levofloxacin pharmacokinetics/pharmacodynamics, dosing, susceptibility breakpoints, and artificial intelligence in the treatment of multidrug-resistant tuberculosis. Clin Infect Dis 67:S293-302
38. Garg RK, Rizvi I, Malhotra HS, Uniyal R, Kumar N (2018) Management of complex tuberculosis cases: a focus on drug-resistant tuberculous meningitis. Expert Rev Anti Infect Ther 16:813–831
39. Juric D, Rohner NA, von Recum HA (2019) Molecular imprinting of cyclodextrin supramolecular hydrogels improves drug loading and delivery. Macromol Biosci 19:1800246

40. Suárez I, Fünger SM, Kröger S, Rademacher J, Fätkenheuer G, Rybniker J (2019) The Diagnosis and Treatment of Tuberculosis. Dtsch Ärztebl Int [Internet]. https://doi.org/10.3238/arztebl.2019.0729 (**cité 6 avr 2022**)
41. Hashemi-Moghaddam H, Kazemi-Bagsangani S, Jamili M, Zavareh S (2016) Evaluation of magnetic nanoparticles coated by 5-fluorouracil imprinted polymer for controlled drug delivery in mouse breast cancer model. Int J Pharm 497:228–238
42. Asadi E, Abdouss M, Leblanc RM, Ezzati N, Wilson JN, 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
43. Griffete N, Fresnais J, Espinosa A, Wilhelm C, Bée A, Ménager C (2015) Design of magnetic molecularly imprinted polymer nanoparticles for controlled release of doxorubicin under an alternative magnetic field in athermal conditions. Nanoscale 7:18891–18896
44. Zhang Q, Zhang L, Wang P, Du S (2014) Coordinate bonding strategy for molecularly imprinted hydrogels: toward pH-responsive doxorubicin delivery. J Pharm Sci 103:643–651
45. Li C, Ma Y, Niu H, Zhang H (2015) Hydrophilic hollow molecularly imprinted polymer microparticles with photo- and thermoresponsive template binding and release properties in aqueous media. ACS Appl Mater Interfaces 7:27340–27350
46. Mao C, Xie X, Liu X, Cui Z, Yang X, Yeung KWK et al (2017) The controlled drug release by pH-sensitive molecularly imprinted nanospheres for enhanced antibacterial activity. Mater Sci Eng C 77:84–91
47. Haupt K (2010) Plastic antibodies. Nat Mater 9:612–614
48. Cutivet A, Schembri C, Kovensky J, Haupt K (2009) Molecularly imprinted microgels as enzyme inhibitors. J Am Chem Soc 131:14699–14702
49. Liu Y, Fang S, Zhai J, Zhao M (2015) Construction of antibody-like nanoparticles for selective protein sequestration in living cells. Nanoscale 7:7162–7167
50. Sankarakumar N, Tong YW (2013) Preventing viral infections with polymeric virus catchers: a novel nanotechnological approach to anti-viral therapy. J Mater Chem B 1:2031
51. Nahhas AF, Webster TJ (2021) The promising use of nano-molecular imprinted templates for improved SARS-CoV-2 detection, drug delivery and research. J Nanobiotechnol 19:305
52. Parisi OI, Dattilo M, Patitucci F, Malivindi R, Pezzi V, Perrotta I et al (2020) "Monoclonal-type" plastic antibodies for SARS-CoV-2 based on Molecularly Imprinted Polymers [Internet]. Synth Biol. https://doi.org/10.1101/2020.05.28.120709
53. Canfarotta F, Waters A, Sadler R, McGill P, Guerreiro A, Papkovsky D et al (2016) Biocompatibility and internalization of molecularly imprinted nanoparticles. Nano Res 9:3463–3477
54. Cazares-Cortes E, Nerantzaki M, Fresnais J, Wilhelm C, Griffete N, Ménager C (2018) Magnetic nanoparticles create hot spots in polymer matrix for controlled drug release. Nanomaterials 8:850
55. Nerantzaki M, Michel A, Briot E, Siaugue JM, Ménager C, Wilhelm C et al (2020) Controlled drug delivery for cancer cell treatment *via* magnetic doxorubicin imprinted silica nanoparticles. Chem Commun 56:10255–10258
56. Boitard C, Curcio A, Rollet AL, Wilhelm C, Ménager C (2019) Griffete N The biological fate of magnetic protein-specific molecularly imprinted polymers: toxicity and degradation. ACS Appl Mater Interfaces 11(39):35556–35565