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Molecular Imprinting: Fundamentals and Applications

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Abstract:

Molecular imprinting technology (MIT) is the technology of composition a molecular lock to match a molecular key that complementary to the template in shape, size, positions and arrangement of the functional groups . Molecular imprinting technology can be used as ideal materials in various application fields ,such as solid-phase extraction (SPE), liquid chromatography, capillary electro chromatography, binding assays and biosensors. The aim of this review paper is to give a fundamental description of the molecular imprinted polymer and to give the reader an insight into the main developments in this technique , Particular emphasis will be placed on their role as affinity materials in chemical/biological sensing, separation science and drug delivery. This review described first general aspects in MIP history and then dealing with various application aspects.

Keywords : Molecularly Imprinted Polymers (MIPs), Molecular Imprinting Technology (MIT), Sensors, Porogens, Drug Delivery**.**

1.Introduction

Molecular recognition is one of the fundamental principles in life. Interest in it has grown substantially during the last three decades, as life uses this strategy to detect both desired and unwanted compounds, which thus makes it the basis of such different phenomena as the immune system

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or cell detoxification [1]. The key to recognition is non-covalent interactions and self-organization[2]. Both are necessary to ensure reversible binding of a target compound to a receptor site. When aiming at artificial, highly functional materials to mimic these natural processes, molecular imprinting technology has become a highly interesting strategy to achieve such functionality in man-made polymers. Molecular imprinting technology (MIT) is today a viable synthetic approach to design robust molecular recognition materials able to mimic natural recognition entities, such as antibodies and biological receptors [3–8]. The design of synthetic materials, which are able to mimic the recognition processes found in nature, has become an important and active area of research . Molecular imprinting are one of the strategies that followed to create materials with recognition ability comparable to the natural systems. MIT is considered a versatile and promising technique which is able to recognize both biological and chemical molecules including nucleotide derivatives [9] ,amino acids , proteins [10–12], drugs , food [13,14] and pollutants [15,16] Further, application areas include: separation sciences and purification [15,17–22] of biological antibodies and receptors system [10,23,24] , drug delivery [25] , catalysis [26], chemical sensors [26,27]. Applications in different chromatographic techniques especially in chiral separations give fundamental insight into the physicochemical properties of the bulk materials used . In sensor science on the other hand very high sensitivity and selectivity of the receptor layer is required, because in sensing only one theoretical plate can be utilized to separate the desired analyte from its matrix .

2 . History of molecular imprinting

The first example of molecular imprinting is attributed to M. V. Polyakov in 1931 with his studies in the polymerization of sodium silicate with ammonium carbonate. When the polymerization process was accompanied by an additive such as benzene, the resulting silica showed a higher uptake of this additive [28]. By 1949, the concept of instructional

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theory of molecular imprinting was used by Dickey; his research precipitated silica gels in the presence of organic dyes and showed imprinted silica had high selectivity towards the template dye [29] , that following Dickey's observations, Patrikeev published a paper of his 'imprinted' silica with the method of incubating bacteria with gel silica. The process of drying and heating the silica promoted growth of bacteria better than other reference silicas and exhibited enantioselectivity [30] . He later used this imprinted silica method in further applications such as thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) . In 1972, Wulff and Klotz introduced molecular imprinting to organic polymers. They found that molecular recognition was possible by covalently introducing functional groups within the imprinted cavity of polymers [31,32] . The Mosbach group then proved that it was possible to introduce functional groups into imprinted cavities through non-covalent interactions, thus leading to non-covalent imprinting [33,34] . Many approaches regarding molecular imprinting have since been extended to different purposes [28] .

3.Types of Molecular Imprinting

The process of molecular imprinting involves the polymerization of a functional monomer and a cross-linker around a molecular template [35] as illustrated in figure (1) .Nowadays,there are three main preparation of MIPs based on covalent , non-covalent and semi-covalent interactions between the template and the functional monomer[36,37].

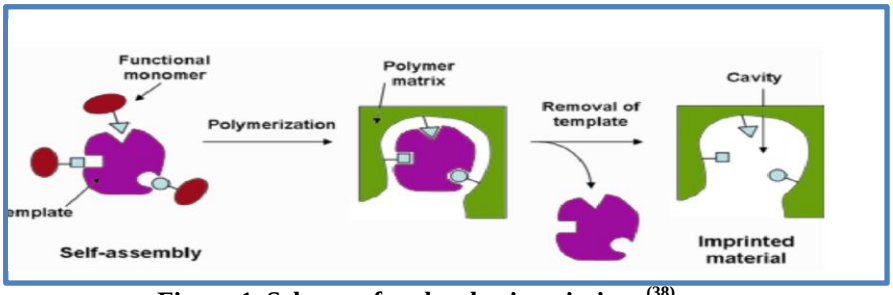

Figure 1. Scheme of molecular imprinting [38]

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3.1 Covalent imprinting

In covalent imprinting, the template molecule is covalently bonded to the functional monomers that are then polymerized together. After polymerization, the polymer matrix is cleaved from the template molecule, leaving a cavity shaped as the template. Upon rebinding with the original molecule, the binding sites will interact with the target molecule, reestablishing the covalent bonds [39,40] (Figure 2) . covalent imprinting is a typical method and often uses readily reversible condensation reactions involving Schiff's base[41] , ketals/acetals [42] and boronate esters[43] However, covalent imprinting is regarded as a less flexible method since there versible condensation reactions are limited. Moreover, it is very difficult to reach thermodynamic equilibrium since the strong covalent interactions will result in slow binding and dissociation [44]

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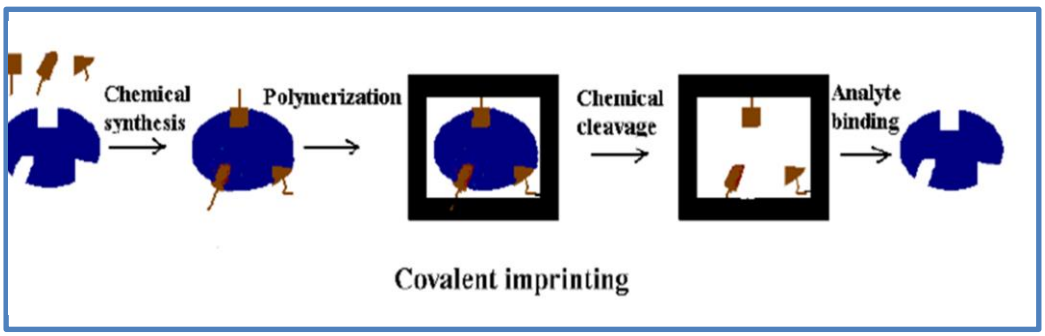

Figure 2. Scheme of Covalent imprinting[39]

3.2 Non-Covalent imprinting

Non-covalent imprinting can proceed by ionic interactions, hydrogen bonding, van der Waals forces and p–p interactions. Most commonly, the dominant interaction is hydrogen bonding, which often occurs between methacrylic acid (MAA) groups and primary amines in nonpolar solvents

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[45]. Recently, non-covalent imprinting has become the most popular and general synthetic strategy due to the simplicity of operation and rapidity of binding and removal However, non-covalent imprinting is sensitive to even slight disruption of the interactions holding the complex together (for example, the presence of water), and it is therefore not very robust [46] (Figure 3).

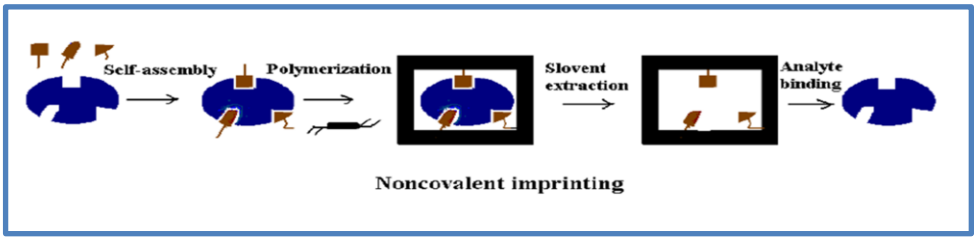

Figure 3. Scheme of Non-Covalent imprinting[39]

3.3 Semi - Covalent imprinting

In order to combine the durability of covalent imprinting and the rapid target uptake of non-covalent imprinting, a new method called semi covalent imprinting has been emerged. This method offers an intermediate alternative in which the template is bound covalently to the functional monomer, but template rebinding is based on non-covalent interactions [47].

4. Essential elements of molecular imprinting

The mixture for an imprinted polymer contains a template (the target analyte), functional monomer and crosslinking monomer (or functionalized crosslinking monomer), porogen and initiator**.**

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4.1 Target compounds/templates

The template molecule ideally should contain at least one functional group through which it can interact with the functional monomer as well a distinctive three-dimensional structure [48]. The type of functional group controls the imprinting approach that can be utilised. Not all templates will readily form a covalent bond with a functional monomer that is easily cleaved. On the other hand the number of functional groups affects the affinity of the template for the molecular imprinted polymer. Increasing the number of interactions between the template and functional monomer may increase the affinity with which the molecular imprinted polymer rebinds the template [49]. However it also increases the non-specific binding of the template to the polymer. Removal of the template after polymerisation is necessary to reveal the imprinted cavities. If residual template remains, these can leak out while performing tests on the polymers. A wide range of target compounds/templates of environmental, biological, pharmaceutical, chemical, industrial and clinical interests (e.g. pesticides, endocrine disruptors, drugs, nucleotides, carbohydrates, steroids and hormones) have been employed as templates in preparation of MIPs. Imprinting biological macromolecules e.g. proteins or viruses, is still a challenging problem, possibly owing to less rigid nature of these macromolecule which resists the formation of well-defined cavities in the crosslinked polymer matrix. The topic has been discussed at length in a recent review article [50]. Besides, organic, ionimprinted polymers for a variety of toxic heavy metals including Al^{3+}, Hg^{2+}, Cr^{3+}, Cd^{2+}, Ru^{3+} and Eu^{2+} have been developed successfully with similar functional monomers and cross-linking agents [51].

4.2 Functional monomer

The careful choice of functional monomer is one of the most importance to provide complementary interactions with the template and substrates. For covalent molecular imprinting, the effects of changing the template to functional monomer ratio is not necessary because the template

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dictates the number of functional monomers that can be covalently attached; furthermore, the functional monomers are attached in a stoichiometric manner. For non-covalent imprinting, the optimal template /monomer ratio is achieved empirically by evaluating several polymers made with different formulations with increasing template [52]. The underlying reason for this thought to originate with the solution complex between functional monomers and templates, which is governed by Le Chatelier's principle. Applying Le Chatelier's principle to the complex formed prior to polymerization, increasing the concentration of components or binding affinity of the complex in the prepolymerization mixture would predict an increase in the pre-polymer complex. Correspondingly, there is an increase in the number of final binding sites in the imprinted polymer, resulting in an increased binding or selectivity factor per gram of polymer.

4.3 Cross-Linkers

Cross-linking allows with the fixation of the functional monomers around the template for the preservation of a rigid polymer structure even after the removal of the template. MIP operation is required an optimized amount of cross-linker . Lowering the amount of cross-linker produces unstable mechanical properties whereas a too high amount leads to the reduction in the number of recognition sites per MIP unit mass. The limited number of possible cross-linkers hinders the progress in MIP technology; hence one of the future directions of research in MIPs is bound to be development of new cross-linkers[53] . Figure (4) is shown of some common cross-linkers used in MIP preparation.

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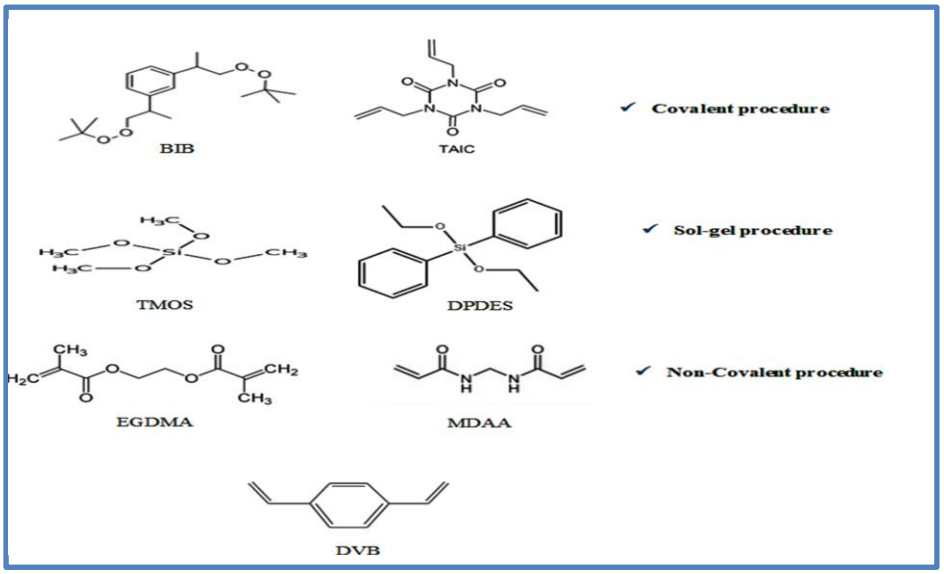

Figure .4 some common cross-linkers used in MIP preparation

4.4 Porogens

Porogenic solvent plays an important role in polymerization. It acts as not only a porogen but also solvent in preparation process. Besides, it also influences the bonding strength between functional monomers and templates the property and morphology of polymer, especially in non-covalent interaction system. Aprotic and low polar organic solvents, such as toluene, acetonitrile and chloroform are often used in non-covalent polymerization processes in order to obtain good imprinting efficiency. It is notable that MIPs prepared in organic solvent work poorly in aqueous media because of the ‘‘solvent memory’’. The influence of solvents has different roles such as it solubilises all the monomers in the pre-polymerisation mixture before polymerisation. It stabilises template monomer pre-polymerisation complex and it acts as a ‘porogen’ helping to control the porosity of the resulting polymer. The range of suitable porogen for a particular molecular imprinted polymer system is limited by the type of interaction between the template and environment. The porogen also

plays a role in forming a porous polymer by acting as a space-filler. It is eventually removed, just like the template, to create channels within the polymer which increases the accessibility of the imprinted cavities [54]

4.5 Initiators

The initiator starts the polymerisation process by providing a source of free radicals. These can be generated by thermal or photolytic decomposition of azobis(nitriles) or peroxides. The temperature of initiation can affect the strength of the complex formed by the reactants before polymerisation. This depends on the interactions between the template and monomer. It is important that the temperature of initiation is lower than the boiling point of the porogen [36,55] .

5. Application of molecular imprinting

5.1 Molecular imprinting in separation techniques

Molecularly Imprinted Chromatography is one of the most traditional applications of molecularly imprinted polymers [56-58] especially for Liquid Chromatography (LC) [59,60] with molecular imprinting polymers usually synthesized by bulk polymerization, ground and sieved mechanically and subsequently packed in a chromatographic column [61] . However, the mechanical processing leads to irregular particles with relatively broad size distribution, resulting in packing of irreproducible quality. For this reason monolithic molecular imprinting columns have been recently prepared directly inside stainless steel columns or capillary columns [62,63] . The monolithic molecular imprinting polymers have fewer nonselective sites than the conventional bulk molecular imprinting polymers particles, even if the polar porogen used for molecular imprinting polymers synthesis can give poorer enantiomeric separation. Many efforts to decrease heterogeneous size distribution have been made also by preparing spherical and monodispersed beads as HPLC stationary phases. Experimental data

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suggest that not always a uniform molecular imprinting polymers particle sizes allow better chromatographic performances. For instance, precipitation polymerization was used to prepare spherical beads but with a total pore volume still lower compared to irregular particles obtained by bulk polymerization and it has been seen that the particles porosity of the beads strongly influences the chromatographic performance of these systems [64] .The first studies were made by Sellergren group that realized an MIP sorbent used as a stationary phase in LC, to separate amino acid derivatives [65] . Daniel and co-worker prepared L-phenylalanine anilide as the print molecule and methacrylic acid as the functional monomer as an important application of molecularly imprinted polymer in anaylical chemistry .Methacrylic acid interacts ionically with the primary amine of the print molecule and via hydrogen bonding with the amide function. In the HPLC mode such polymers were shown to exhibit efficient enantiomeric resolution of a racemic mixture of the original print molecule [66] . Sellergren and co-workers prepared an acrylic polymer by non-covalent imprinting procedure for selective enantioseparation of D or L-Phenylalanine ethyl esters to evaluate the enantio and substrate-selectivity for some amino acid derivates [67] . In early days , optical resolution of chromatography applications are carried out by the stationary phase either a chiral material or chiral selectors coupled to a non-chiral support material. Now a day's molecular imprinting, has gained increasing interest for the preparation of chiral stationary phases. There are lots of work was performed on the chiral separation [68,69] . Molecularly imprinted materials have been employed as chiral matrices in different separation techniques. Chirality may be introduced into polymer matrices starting in most cases from chiral building blocks. This chirality is thus a consequence of the asymmetry carried by the template [70-73] . A characteristic of imprinted chiral stationary phases for chromatography is the predetermined elution order of the enantiomers, which depends only on the enantiomers used as the template molecule. For instance, if the D-enantiomers is used as the template, it will be retained more by the polymer than by the L-

enantioners, and vice versa. The discrimination of enantiomers is often very efficient with molecularly imprinted materials yielding highly efficient chiral separations [74,75] . Researchers successfully prepared 4-nitrophenol imprinted polymer by a thermal polymerization method by using 4-vinylpyridine (4-VP) and ethylene glycol dimethacrylate (EDMA) as a functional monomer and crosslinker, respectively and they discussed its application as stationary phase for HPLC measurements . Furthermore, the specific binding sites that have been mated during the polymerization process were analyzed via radioligand binding assays. The successful imprinting against 4-nitrophenol provides a new opportunity for advanced separation materials used in environmental analysis [76] . Molecularly imprinted polymers (MIPs) have been prepared by spherical and monodispersed methods in micrometer sizes with using suspension polymerization in water , liquid perfluorocarbon and mineral oil, seed polymerization or dispersion/precipitation polymerization. Molecularly imprinted polymers microspheres were successfully applied for parmaceutical , biomedical and enviromental analysis as affinity-based chromatographic media [77] . In 1996,Membranes prepared as freestanding thin films or thin polymer films on the surface of solid supports following standard imprinting recipes[78] . In other study , the author found a different approach towards the development of molecularly imprinted polymer membranes. MIP was synthesized in the pores of polypropylene membranes to obtain mechanically stable membranes for preparative application. The amino acid derivative CBZ tyrosine was chosen as the target molecule, and a standard polymer recipe for non-covalent imprinting was used [79] . Lei Ye et al., reported preparation of extremely stable and specific adsorbents for the product ZL-Asp-L-Phe-OMe (Z-aspartame) using the emerging technique of molecular imprinting. This new methodology may be used in various synthetic applications such as high pressure and temperature stability, allowing molecular imprinting polymers to withstand sterilization conditions [80].

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5.2 Molecular imprinting as chemical sensors and biosensors

The astonishing development of biosensors in chemical and biological sciences is due to their incredible specificity and assorted applications [81]. In the last years, chemical sensors and biosensors are of increasing interest in the field of modern analytical chemistry, as can be seen from the growing number of published papers. This is due to new demands which appeared particularly in clinical diagnosis, environmental analysis and also in food analysis. lately, number of significant advances have been made to synthesize artificial receptors capable of binding a target analyte with comparable affinity and high selectivity to natural antibodies or enzymes has been done. MIT can also be used as antibody-like materials with high selectivity and sensitivity, owing to their long-term stability, chemical inertness and insolubility in water and most organic solvents [82]. To date, molecular imprinting polymers have been successfully used with different types of transducers and several methods have been used to achieve a close integration of the transduction platform with the polymer [83] . In particular, the integration of molecular imprinting polymers with sensors can be realized by in situ polymerization, using a photochemical or thermal initiator [84] , or by surface grafting with chemical or UV initiation [85,86]. The advantage of this latter approach lies in the possibility of controlled modification of inert electrode surfaces with thin films of specific polymers. Moreover, polymers can also be electropolymerized on the surface of transduction platform. In this case, there are some adhesion problems, especially during the washing process of the polymerized MIP-coated QCM (Quartz Cristal Microbalance) with organic solvents that, sometimes lead to a partly peeling off of the molecular imprinting polymers layers produced. For this reason, specific pretreatment to enhance the adhesion of molecular imprinting polymers on transducer platforms, must be done. The first generation of molecular imprinting polymers sensors were prepared using imprinted polymers synthesized in the form of monoliths. The obtained molecular imprinting polymers particles were deposited in close proximity to the electrode by

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incorporation of the particles into the carbon paste of screen-printed electrode [87] or into a supporting agarose gel [88] . It was observed that the response of the sensor was strongly dependent on how intimately the molecular imprinting polymers and transduction element were integrated and how efficient the electrical communication was between them Competitive amperometric morphine sensor using molecular imprinting polymers particulates immobilised with agar gel on the electrode surface, has been reported by Mosbach's group [89]. The thickness of the film deposited on the transducer is important to obtain a good time response of the sensor. This approach was firstly used with acoustic [90] and optical [91] transducers and then with electrochemical sensors [92]. Today, a simple approach to obtain sensor device, is the combination of molecular imprinting polymers with a piezoelectric transducer (e.g., quartz) to create an acoustic asensor called QCM-MIP sensor. The coating of the crystal with the molecular imprinting polymers can be obtained by in situ polymerization directly onto the surface of the device [93,94] or via pre-prepared molecular imprinting polymers particles that are immobilized on the sensor surface using a PVC matrix [95] . Moreover, a sorbitol-based molecular imprinting polymers was also prepared by electropolymerization of o-phenylenediamine on a QCM surface [96] . In another study, an imprinted polymer-coated sensor was created by Tan et al. to determine the amount of paracetamol and nicotine in biological fluids [97,98] . Recently, Ersőz and co-workers have developed a new QCM sensor for specific determination of 8-hydroxy-2'-deoxyguanosine (8-OHdG), an oxidative stress marker [99] . The molecular imprinting polymers was prepared by in situ polymerization of methacryloylamidohistidine-platinum(II) and N-N'-methylenebisacrylamide on QCM surface and used to determine the amount of (8-OHdG) in the blood of cancer patients. QCM-MIP sensor was also realized for detection of daminozide, a potential carcinogenic chemical important in food safety [100] and also for detection of environmental pollutants such as bisphenol A [101] , acetaldehyde [101] and monoterpenes [102] . Molecular imprinting polymers were also widely

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employed as sensors for enantiomeric separation of different compounds such as R and S-propranolol, D and L-tryptophan, and D and L-serine enantiomers [95,103,104] . Several efforts to adapt molecular imprinting polymers-based QCM sensing technology to chiral recognition of (S)-propranolol have been reported by Haupt and co-workers that created an enantioselective chiral recognition layers. on the gold-coated surfaces of 5 MHz quartz crystals employing a poly(TRIM-co-MAA) molecular imprinting polymers formulation [95] . Recently, Ye et al. synthesized (R,S)-propranolol imprinted microspherical beads by a modified precipitation polymerization and they were used in competitive radio-labeled MIAs for chiral analysis of propranolol, using (S)-[4-3H]Propranolol as radioactive probe. When the molecular imprinting polymers was used in scintillation proximity assays, the binding of the radio-labeled template determined a transfer of energy from template to scintillant resulting in the generation of a fluorescence signal [105] . In another study, 17β-estradiol imprinted beads prepared by precipitation polymerization were employed in a competitive radio-labeled MIAs to obtain a stereoselectivity for 17β-estradiol over its diasteroisomer 17α-estradiol [106] . Nevertheless, the practical applications of this technology are heavily restrained due to the inherent complications of handling and disposing of radioactive materials. For this reason, fluorescent analogues of analytes were employed as alternative probes in MIAs. Conventional fluorescent-labeled MIAs is an example of non-homologous assay where the molecular imprinting polymers is prepared using the analyte itself as template in the imprinting process and a fluorescent probe in place of the radioactive probe. However, a problem that hinders the development of this technique is due to different structures of the fluorescent probe, which has additional fluorescent groups to that of the analyte, inducing a decrease of sensitivity and selectivity. Nevertheless, in the last few years, many researchers have focused their interest on fluorescence -labeled MIAs [106–110] primarily for their attractive practical features in future applications.

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5.3 Molecular imprinting in drug discovery

The ability MIP to bind strongly and selectively to bioactive molecules makes these materials suitable for their potential application in biological field. The high loading capacity and the prolonged release time of the analytes, such as drugs, amounts to MIP having a huge potential for creating suitable dosage forms [(111)] . Development of a number of significant have been made new technologies to maximise the efficacy , safety of medicines and also for optimising drug delivery in the last decade [(112)] . Drug delivery systems (DDS) must be capable of regulating the rate of release (delayed- or extended-release systems) and/or targeting the drug to a specific site. Efficient DDS should provide a desired rate of delivery of the therapeutic dose, at the most appropriate place in the body, prolong the duration of pharmacological action reduce the adverse effects, minimise the dosing frequency and enhance patient compliance. To control the moment at which delivery should begin and the drug release rate, the three following approaches have been developed [(113)] (i) drug diffusion from the system has to follow a specific rate profile; (ii) The release is activated by some physical, chemical or biochemical processes ; and (iii) the rate of drug release is regulated by the concentration of a triggering agent, such as a biochemical substance, concentration of which is itself dependent on the drug concentration in the body. molecular imprinting polymers for drug delivery applications should have specific characteristics: the imprinted cavities should be stable to maintain the conformation in the absence of the template, but also flexible to facilitate the realization of a fast equilibrium between the release and re-uptake of the template in the cavity. To this end, the non-covalent imprinting provides faster equilibrium kinetics than the covalent imprinting approach. Furthermore, molecular imprinting polymers should be stable to resist enzymatic and chemical attacks and mechanical stress that can be found in biological fluids [(115)] . The Molecular Imprinting polymers are normally synthesized in organic solvents to improve hydrogen bonding and

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electrostatic interactions [116] . The presence of organic solvents, commonly used in molecular imprinting polymers synthesis, may cause cellular damages. For this reason, in drug delivery processes, it is usually advantageous to prepare hydrophilic polymers which are compatible with biological systems. Nevertheless, precipitation polymerization method can be used since the polymer is usually completely immiscible with the solvent used for Molecular Imprinting polymers preparation allowing easy polymer separation from the solvent [117]. MIP water compatible is still under development and there are many problems due to the considerable weakness of hydrogen bonding and electrostatic interactions in water that decrease the selectivity of the Molecular Imprinting polymers for the target molecule. However, metal coordination and hydrophobic interactions can be exploited to enhance template and functional monomer interactions [118,119] . The first report of imprinted polymers used as sustained release devices has been presented by Norell and co-workers [120] .Similar results were obtained with other drugs, such as tetracycline [121] and sulfasalazine . Cai and Gupta using tetracycline as a template for synthesis of MIP with higher binding ability compared with corresponding non-imprinted polymers. The obtained results indicated that the high Molecular Imprinting polymers affinity can be utilized in control release applications, in fact the tetracycline release from MIP was slower than non-imprinted polymer [122]. In another study, molecularly imprinted polymers (MIPs) have been used as unconventional synthetic polymeric carriers, to prepare drug delivery systems for sustained release of NAM molecules. Controlled NAM release systems are useful to extend the duration of the drug's pharmacological activity and to minimize administration frequency. [123]. A system with similar characteristics, able to release testosterone at a rate depending on the concentration of hydrocortisone, was described by Sreenivasan et al. In this study, hydrocortisone as template was used for the preparation of Molecular Imprinting polymers. After the removal of target analyte, the molecular imprinting polymers was loaded with testosterone, which is a structurally similar MIPs. It was seen that the rate

of testosterone release increased when hydrocortisone was present in the solution as a result of template responsive release [124] . MIPs can be used also to bind several substances in the gastrointestinal tract, blocking their absorption in the body, as a complement of the pharmacological therapy. In this contest, molecular imprinting polymers as chemical traps to remove undesirable substances from the body, such as glucose, cholesterol [125,126,127] . bile acid [128] and melatonin [129] were developed. Hoshino and coworkers. prepared imprinted polymers nanoparticles able to efficiently capture the cytotoxic peptide melittin in the bloodstream, synthesizing protein-size polymer particles with a binding affinity and selectively comparable to those of natural antibodies, by combining molecular imprinting polymers nanoparticle synthesis with a functional monomer optimization strategy [129] .

6. Conclusions

This review has attempted to outline various aspects of molecular imprinting technologies. excellent stability , Low cost and continuously advancing performance of Molecular Imprinting polymers make these polymers the most promising synthetic materials for molecular recognition in different scientific fields. Molecular Imprinting polymers have been widely studied as HPLC stationary phases , especially for chiral Stationary Phases in High Performance Liquid Chromatography . However, an increasing number of papers on Solid-phase extraction (MISPE) have been produced. Solid-phase extraction is a competitive analysis procedure for the stability and low cost preparation of the imprinted materials, compared with traditional solid-phase extraction. Today there are already Solid-phase extraction cartridges commercially available for selective extraction of several molecules. Molecular Imprinting polymers attention has been directed to the development of Molecular Imprinting as selective material for biosensors and sensors . In terms of Molecular Imprinting polymers-based biomimetic sensors is still rather inferior to biosensors because they require further optimization of the Molecular Imprinting polymers and the

transducers. Thus, although the stimulating ongoing work in this field, the commercial development of molecular imprinting sensors is still in its infancy. Drug delivery applications has not yet been thoroughly investigated. Applications in this areas are only just beginning to emerge and there are several potential aspects to be explored that could produce progress in the next few years.

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