

The Development of Molecularly Imprinted Polymers in the Clean-Up of Water Pollutants: A Review

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Abstract

In the last decades, the extensive use of chemical and biological materials has not only seen to an increased transport of environmental pollutants but also, it has interfered and compromised the pristine state of different environmental matrices with emphasis on waterbodies. This has stimulated studies to develop and adopt novel techniques which consider the removal of pollutants with premium on economic feasibility, simple instrumentation, and high performance. In the treatment of water, the removal of trace concentration organic compounds and other numerous polluted water effluents is difficult due to limited affinity of trace compound ions to ion exchange resins. Because of the selective nature; recognition properties; adsorption ability; high stability; and easier preparation of molecular imprints, they are considered attractive and suitable artificial receptors to be applied in analytical separations, drug delivery, and as chemical sensors. In this review, we touch on the fundamentals of molecularly imprinted technologies and underscore some recent advances made in the development of imprinted polymers that are compatible with water and how they can be used in the clean-up of pollutants. The paper finally presents a comprehensive report on some challenges and outlook in the use of MIPs as water treatment sorbent.

Keywords

Wastewater Treatment; Aqueous Conditions, Molecularly Imprinted Polymers, Water-Compatible

1. Introduction

Water is and remains a fundamental requirement for the sustenance of almost

all organisms starting from the simplest to the most complex plant and animal. The use of water by plants during photosynthesis and the dependency of animals on the food prepared by plants invariably make water an indispensable commodity and a life supporting resource. Water plays a significant role in all biological association [1] and it circulates through all living organisms: plants, animals and human beings all use water for very important and specific reasons. In essence, water bathes and feeds the human existence and the world basically runs on water.

Nevertheless, the escalating pace with which urbanization, industrialization, and other anthropogenic activities have increased over the years has polluted and depleted the pristine state of fresh water resources: this has altered demand and supply relationship of freshwater in some countries with millions of people dying each year [2]. Many developing countries are already struggling to meet supplies of daily water needs and the inadequacies of their existing water infrastructure [3]. In order to augment and bridge discrepancies in demand and supply of freshwater with respect to quality, quantity, sustainable supplies, and environmental protection, an alternative source of water worth considering is treatment of polluted water and reuse [4].

Technologies that enhance treatment and purification of water use several different purification methods in order to thoroughly clean polluted water. Prominent of these methods are: nano-filtration [5]; bioremediation [6]; chemical sedimentation [7]; coagulation [8]; and oxidation [9]. Unfortunately, these methods are not always effective for the enough removal of trace concentrations organic compounds and other numerous polluted water effluents [10].

These micro-pollutants and organic compounds are mostly man-made substances used in consumer products; agriculture; and electronics and are found in the environment. These artificial compounds, particularly EDCs, have tendencies to mimic, block, or interfere with normal functioning of the body's endocrine system because of their strong potential to bind to estrogen or androgen receptors [11]. They are hence considered lethal and can directly or indirectly provoke hepatotoxicity, endometriosis, abnormalities in sex organs, and carcinogenic diseases [12] [13].

Since water safety is of mandatory importance coupled with the above-mentioned threats posed by EDCs, there is a need to fabricate sensors that can both detect and adsorb these pollutants thus ensuring that pollutants at trace concentration are not found at levels detrimental to human health. Recently, the development of molecularly imprinted polymers has become a promising candidate in water treatment due to their high affinity and specificity for target template. The use of imprinted polymers in the treatment of polluted water could be an efficient technique to detect and selectively remove trace pollutants more effectively, which will in turn improve water treatment in general.

In this review work, a general overview on MIPs with respect to various synthesis approaches, polymerization techniques, and some parameters that affect MIPs synthesis will be presented. Premium will be given to how water-compatible

MIPs can be synthesized and used as sorbent in the treatment of polluted water. The final aspect of the paper will give a comprehensive summary of some challenges and outlook in the use of MIPs as water treatment sorbent.

2. Molecular Imprinting Polymers and Synthesis Techniques

The history of molecular imprinting dates to the novel work of Dickey [14], on the imprinting of silica gels. Dickey's work had given molecular imprinting some considerable amount of recognition, but it was not until the concerted efforts of Wulff [15] and Mosbach [16] that molecular imprinting came into the limelight.

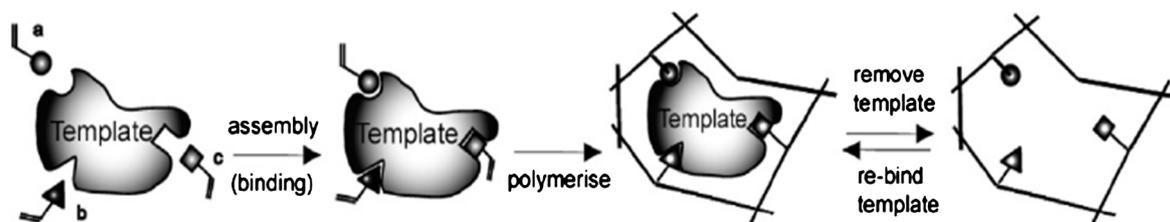
This guest-host technique of molecular imprinting allows the incorporation of specific substrate recognition into a synthetic polymeric matrix. In the process of imprinting, functional monomers are copolymerized with a crosslinker in the presence of template molecule. The polymerization process allows a strong and complex integration of both functional monomers and template to form a rigid polymeric matrix. The resultant polymer matrix after it has undergone a thorough washing and elution are left with cavities similar in spatial arrangement and molecular interaction of template molecules thus its high affinity, selectivity and recognition toward target template.

Concisely, the technology of molecular imprinting leads to replication of macromolecular structure able to demonstrate the very characteristics of parent macromolecular structure with high specificities.

2.1. Synthesis of Molecularly Imprinted Polymers

The concept of imprinting molecular polymers drives largely on the lock-and-key or antibody-to-antigen principles [17]. In synthesizing MIPs, as illustrated in **Figure 1**, there is pre-arrangement of the functional monomers; the polymerization of functional monomers-template complex and cross-linker molecules and the elimination of template molecule from the polymeric structure by way of washing [18] [19] [20]. In paying cognizance attention to the interaction that goes on between monomers and templates during formative stages, three distinct methodologies have been employed: the formation could be done in a covalent, semi-covalent or a non-covalent fashion.

Molecular covalent imprinting or pre-organized methodology pioneered by Wulff *et al.* [22] introduces molecular affinity in organic polymeric complexes where there is reversible covalent bond of templates and functional monomers.



Ref. [21].

Figure 1. Schematic representation of the molecular imprinting process.

In this chemical coupling, there is first a synthesis of a template-monomer complex at the pre-polymerization stage before the main stage of polymerization. Template is cleaved from the polymeric matrix at the end of polymerization to obtain recognition cavities. Owing to the possibility to control the stoichiometry of imprint materials, covalent imprinting has an ultimate advantage of definite, stable, and homogenous binding sites [23]. To their disadvantages, it is difficult to thoroughly remove bonded template from the cross-linked polymeric matrix due to strong bonding chemical interactions between template and monomers and, they exhibit slow association kinetics [24]. Finally, this synthesis technique is somewhat difficult to carry out.

In contrast, non-covalent imprinting does not make use of covalent bonds and it is considered the most effective and widely used approach [25] [26]. The non-covalent interaction such as electrostatic forces (including ion-dipole and dipole-dipole), metal chelate, hydrogen binding, and van der Waals forces ensures that there is appropriate self-assembly and combination of functional monomers and template. After the template through extraction with solvent has been removed, the polymeric matrix is preserved without further bond cleavage and rebinding takes place through the same non-covalent interactions [27]. The non-covalent imprinting approach with its simplicity, inexpensive way of preparation has the advantage of high recognition sites. However, it is not free of some drawbacks such as template bleeding and low-selectivity binding sites.

Another synthetic protocol is semi-covalent imprinting. In this approach, MIPs through covalent interactions are hybridized but template rebinding is entirely non-covalent because of the reversible bond [28]. It has both advantages of covalent and non-covalent imprinting procedures.

Table 1 gives a summary of the specific interactions between template and the functional group in a polymeric network.

Table 1. Approaches employed in molecular imprinting.

| | Advantages | Drawbacks |
|---------------|--|---|
| Covalent | Formation of better defined and more homogeneous binding sites. Polymerization ensures the maximization of the number of specific binding sites | Difficulty in template removal and rebinding. |
| Semi-covalent | Random distribution and association of functional monomers to template molecules. Production of uniform recognition sites. | There may be template bleeding when hydrolysis is unable to remove template. |
| Non-covalent | Experimental simplicity. Easy removal of the template under mild conditions. Fast template binding and release kinetics. Similarity to natural process. | Weak average affinity of binding site. Formation of Nonselective binding sites as a result of random incorporation of excess monomers into the polymer matrix. Strong solvent influences: less polar solvents facilitate hydrogen bonding; more polar solvents facilitate stronger nonpolar interactions. |

2.2. Polymerization Techniques

2.2.1. Traditional Polymerization

It is important to indicate that, MIPs depending on their final application may be prepared using different methods and techniques. Traditionally, the most commonly and easily used imprinting technique is bulk polymerization because of its simple and efficient use on laboratory scale. When MIPs are obtained from bulk polymerization, the resultant polymer monoliths are crushed and sieved into suitable particle size with respect to the purposes of application. The drawbacks of this method may arise when sharp-edged, irregular MIP bits with lower loading capacity and recognition ability are produced: this largely emanates from destruction of interaction sites during grinding [29]. The irregular shape of MIP bits produced by bulk polymerization restricts their usage especially in complex applications [30]. In addition to the challenges, it is time-consuming [31], tedious [32], and has poor binding sites [33].

In order to overcome these drawbacks without necessarily grinding and sieving MIP particles, alternative methods to prepare different MIP formats have been proposed and developed in recent years [34]. Additionally, strategies like surface imprinting have also been employed. Although these techniques have great value in covering up some gaps of TP, it should be noted that their optimization as experimental protocols could somewhat be difficult, lengthy and sometimes questionable in real time application [35].

2.2.2. Precipitation Polymerization

Precipitation polymerization, the most widely used polymerization method with respect to overcome drawbacks of TP is a robust technique of synthesizing polymers in the form of micro- and nano-spherical beads. The technique of precipitation polymerization is no different from bulk polymerization, only that there is much higher amount of porogen in the mixture. In the process of polymerization, polymer chains do not polymerize together but instead, precipitate out of the solution in order to mix and form a polymer monolith [36]. Precipitation polymerization is unique in the preparation of MIPs, in that, it is surfactant-free in nature and produces a high-quality micron-sized particulate [37]. It is however considered expensive and may raise some environmental concerns due to the considerable amount of porogen needed for this technique to be carried out [38].

2.2.3. Suspension Polymerization

Suspension polymerization ensures a uniform production of polymer beads and it is considered as one of the easiest polymerization techniques. In this method, involved monomers are either insoluble or partly soluble in water to ensure monomers insolubility after polymerization. The method also involves the dispersion of monomers to ensure polymerization is carried out inside droplets of monomers [39] [40]. The unlimited and excellent transfer of heat is considered as the biggest advantage of this technique and as such suitable for industrial

scale-up. The number of binding sites, however, may be reduced because of the use of aqueous solution as a dispersing agent. Additionally, water may impede reaction kinetics of template molecule and functional monomers.

2.2.4. Multistep Swelling Polymerization

Multistep swelling polymerization is one way through which polymers can be fabricated. This method pioneered by Hosoya and coworkers [41] with subsequent improvement by Haginaka and Sagai [42] is used in the production of monodisperse particles with controlled diameter in ranges of 2 - 50 μm . The size of monodispersed particles using this technique is slightly higher than those prepared by means of precipitation thus considered ideal for HPLC. This technique however is considered time-consuming, requires complicated procedures and reaction conditions, and may have lower performance in the final product [37] [38].

2.3. Critical Parameters in MIPs Synthesis

The guided decision in the selection of parameters needed in the fabrication of imprinted polymers is very imperative since they go a long way to affect the morphology, chemical behavior, and performance of synthesized MIPs [43]. However, the comprehensive understanding of these parameters could be difficult to achieve. Attending to literature, some parameters that influence the success of imprinting process and applications are highlighted in this section.

2.3.1. Functional Monomer

The formation of exact cavities either covalently or non-covalently during the process of polymer synthesis is partly dependent on the choice of functional monomer. Therefore, careful consideration is needed during the selection of functional monomer in targeting a template molecule [28]. Again, the effectiveness of MIPs' recognition site is contingent on the amount and quality of monomer selected to undergo pre-polymerization [44]. Functional monomers noted to have a wide range of usage may include Trifluoromethacrylic acid (TFMAA), 2- or 4-vinylpyridine (2- or 4-VP), and methacrylic acid (MAA). Priority is however given to MAA due to its ability to interact both covalently and non-covalently [45]. In order to enhance performance and selectivity of MIPs, a monomer may sometimes be combined with another monomer [46] [47]. **Figure 2** presents some examples of commonly used monomers for MIPs production.

2.3.2. Cross-Linker

The cross-linker does not only play the role of dictating the morphology of the polymeric matrix but also ensures that functional groups are well positioned with adequate cavities and rigidity [48] [49]. Generally, MIPs with high ratios of crosslinker are preferable in order to ensure desirable features of mechanical stability and rigidity. MIPs prepared from trifunctional cross-linkers, have been observed to give more rigidity, load capacity, and efficiency than EGDMA [50]. In addition, the type of cross-linker is a determinant of the quality and yield of

MIPs after polymerization. TRIM in a study was observed to give higher yield and finer imprinted particles as juxtaposed to divinylbenzene which had a lower yield of MIP particles [51]. **Figure 3** presents some examples of common and extensively used cross-linking agents for MIPs production.

2.3.3. Porogenic Solvent

The important role porogens play in the fabrication of MIPs cannot be underestimated. The environment that ensures polymerization of all MIP synthesizing-

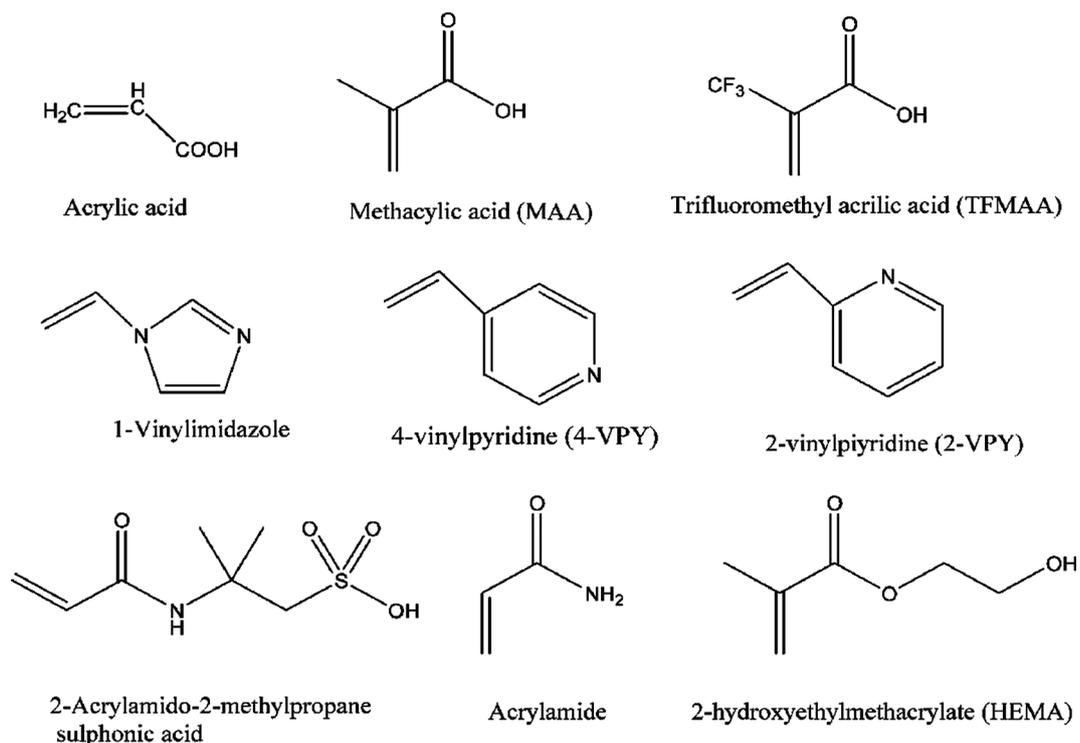


Figure 2. Structure of commonly used monomers for molecular imprinting.

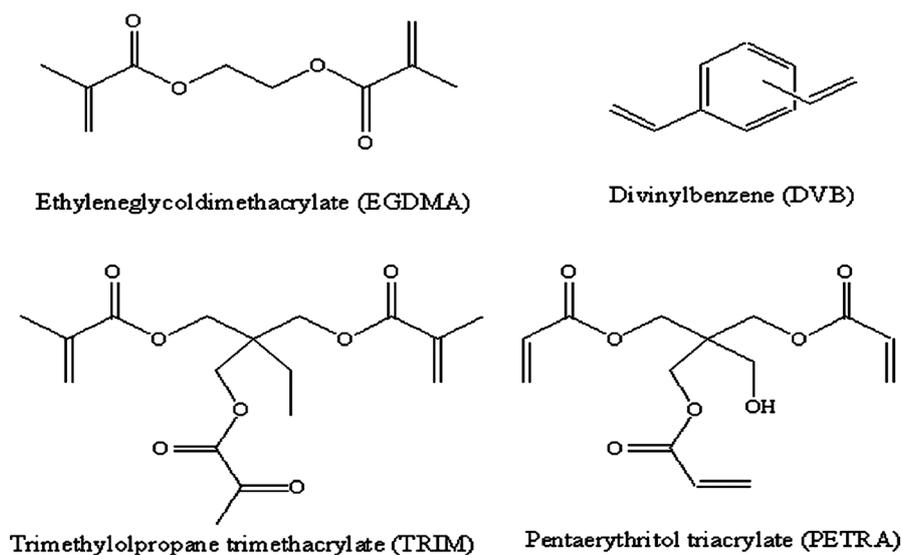


Figure 3. Structure of commonly used cross-linkers for molecular imprinting.

components is created by the solvent. Porogens ensures that, important features such as hydrogen bond formation and surface area are regulated in the pre-polymerization complex. Porogens are responsible for the creation of cavities in the polymeric matrix. Pore sizes are direct function of the nature and solubility of porogen used: low soluble porogens separates faster and creates larger pores sizes as juxtaposed to porogens with high solubility [52].

Additionally, the nature of the porogen employed for the rebinding step will influence activities associated with relative swelling of the polymer [53]. Apolar and non-protic solvent (e.g. chloroform and toluene) may be employed in the synthesis of MIP. In cases where there is involvement of hydrophobic forces, Premium will be given to water and other protic solvents in the synthesis of MIP [50].

2.3.4. Temperature

In order to ensure the effective performance of imprinted polymers in selective detection or adsorption of a target pollutant, it is very important to consider polymerization temperature. Usually, selectivity of MIPs tends to increase when synthesized at lower temperature as against polymers fabricated under higher temperatures. During polymerization at lower temperatures, there is stability of template-monomer complex: this enhances the creation of larger binding cavities. Mosbach's study on enantioselectivity of 1-PheNHP established an increased and better selectivity of polymers at a lower temperature as juxtaposed to polymers polymerized under higher thermal conditions [54] [55].

2.4. Molecularly Imprinted Polymers in Selective Solid-Phase Extraction

The selective removal of compounds and analytes from fluids and aqueous samples has been successful by placing premium on the application of solid phase extraction (SPE). Over the years, scientist and researchers have achieved considerable success in the selective adsorption of target pollutants from environmental waters [56], sediments [57], soils [58], and other complex matrices through the development and application of molecularly imprinted solid phase extraction (MISPE) [59]. The principles of MISPE are basically: Conditioning, which ensures that MIP particles are treated with adequate solvent to get imprinted cavities activated; Loading of sample which allows liquid phase containing the analyte to get into contact with the sorbent; Washing which is the step that ensures that undesired impurities or compounds that interfere with MIP are removed before it gets to the step of Elution which disrupts analyte-MIP interactions by means of a suitable solvent.

In terms of application, MISPE can be applied both in an off-line mode or on-line mode. Owing to the reduction in the adulteration of MIP particles as well as loss reduction of analytes, on-line procedure coupled with HPLC is ideal over off-line mode which situates MIP particles between two frits [37] [60]. However, it is important to stress that MISPE has been used extensively in the

off-line mode as a result of its simplicity of operation and easiness in handling solvents with no bearing to their influence on successive separation methods [61].

3. MIPs in Waste Water Treatment

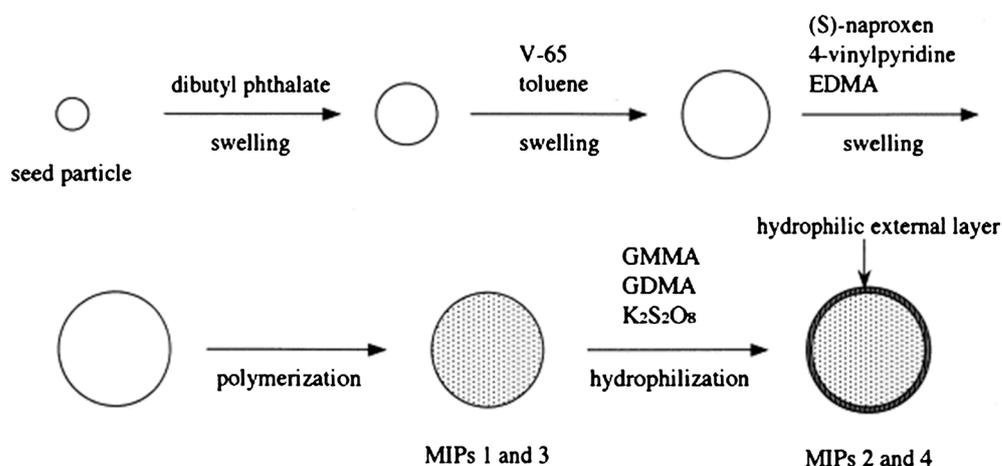
3.1. Development of Water Compatible MIPs

The state of stability and firmness of bonds that exist between functional monomers and template during the synthesis of imprinted polymers is defined when the process takes place in low polar organic or aprotic solvent [60]. However, one of the challenges scientists of imprinted polymers face must consider the extensive application of imprinted polymers in inorganic solvents [62]. MIPs tend to exhibit different character when measured in organic and inorganic solvents [63] thus the anomaly of uneven swelling and non-specific binding shown when applied in water. To ensure effective and selective removal of contaminants in polluted water, it is imperative to imprint polymers that are compatible with water and at the same time have defined monomer-template strength. The following part of this review underscores works that have been conducted in the improvement of water-compatible MIPs.

3.2. Development of Water-Compatible MIPs Using Surface Post-Modification

The predominance and interference of water with template-monomer bonds lead to uneven swelling and non-specific adsorption of MIPs in aqueous solution. In order to increase adsorptive selectivity, chemical modification or grafting polymer layers onto surfaces of molecularly imprinted polymers have proven useful over the years.

The surface coating of MIPs using a restricted access hydrophilic layers by Haginaka *et al.* ensured the control of non-selectivity adsorption which was stimulated by the exchange of ions between functional monomers and templates as shown in **Figure 4** [64]. The surface of monodispersed MIP particles which were



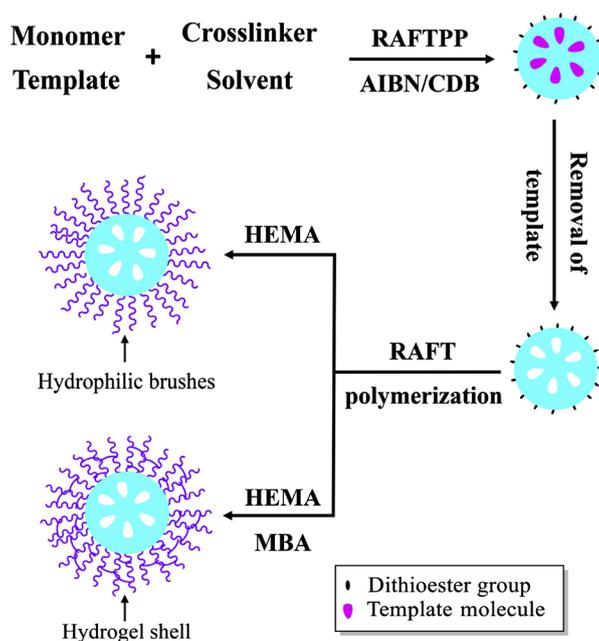
Ref. [64].

Figure 4. A schematic representation of modified MIP for (S)-naproxen.

designed for the selective adsorption of (S)-naproxen were modified when Haginaka *et al.* primarily coated the surface microspheres with a hydrophilic external layer of glycerol monomethacrylate (GMA) and a subsequent modification of glycerol dimethacrylate (GDMA) using a multi-step swelling and polymerization method. The study indicated modified MIPs to have better adsorption recognition of template as juxtaposed to unmodified particles. The use of this technique has enhanced the reduction of nonspecific binding with followed-up studies indicating how it could be directly applied to analyze (S)-ibuprofen in serum and β -blockers in biological fluids [65] [66].

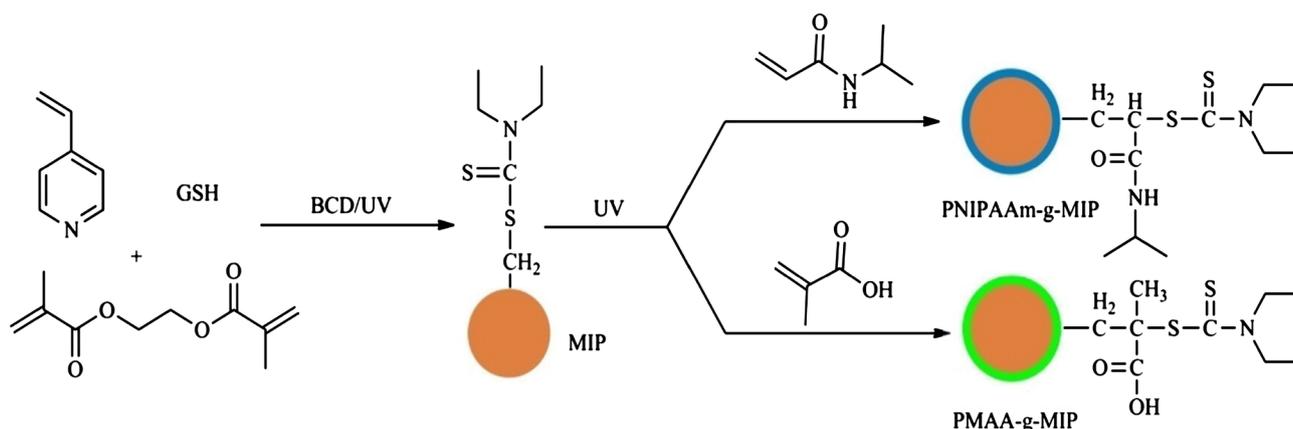
In order to suppress hydrophobic interactions by way of grafting polymer brushes of poly (2-hydroxyethyl methacrylate) (HEMA), Zhang *et al.* [67] were able to enhance specific determination of templates in aqueous environment. Through surface-bonded RAFT, the group was able to synthesize the MIP core with a later synthesis using hydrophilic polymer brushes. The binding selectivity of the MIP/NIP microspheres after measuring their competitive binding capacities towards 2,4-D and its structurally related compound POAc was established, indicating MIPs high selective performance in aqueous media. **Figure 5** gives a schematic illustration of the synthesis process. **Figure 5**: Schematic illustration for the controlled synthesis of hydrophilic MIP using RAFT polymerization:

Similarly, the introductions of ultrathin polymer brushes onto MIP microspheres were observed to improve the performance of water-compatible MIP designed toward the adsorption of glutathione template compounds [68]. Through controllable surface-graft polymerization which is shown in **Figure 6**, polymer brushes of *N*-isopropylacrylamide were grafted onto the MIP particles.



Ref. [67].

Figure 5. Schematic illustration for the synthesis of hydrophilic MIP using RAFT polymerization.



Ref. [68].

Figure 6. Schematic illustration for the controlled synthesis of MIPs toward glutathione determination.

Using high-performance liquid chromatography for the peak separation and UV spectrophotometer for the absorption spectra, it was seen that, templates in aqueous solution were selectively adsorb per grafting modification.

Elsewhere, in a solid-phase technique which ensured the chemical deposition of hydrophilic polyethylene glycol onto the surface of MIP particles, Moczko *et al.* were able to enhance the recognition and selectivity ability of MIP polymers [69]. Using surface plasmon resonance (SPR) tests to confirm if the molecular recognition properties of the core-shell NP remained unaffected by the grafting of the polyethylene glycol shell, it was shown that, the surface-imprinted NPs was not affected by grafting and had an excellent affinity and specificity at 36 °C. Another study carried out by F. Puoci showed that, the unselective detection of target template significantly reduced when glycidyl methacrylate (GMA) as a co-monomer was coated as hydrophilic layer onto MIPs [70]. Similarly, Manesiotis *et al.* through the introduction of hydrophilic layers by way of alkaline post modification treatment onto MIP layers were able to selectively remove riboflavin from beverage [71]. As this chemical treatment ensured the reduction of nonspecific binding, it also ensured that the performance and binding cavities of MIP layers were maintained.

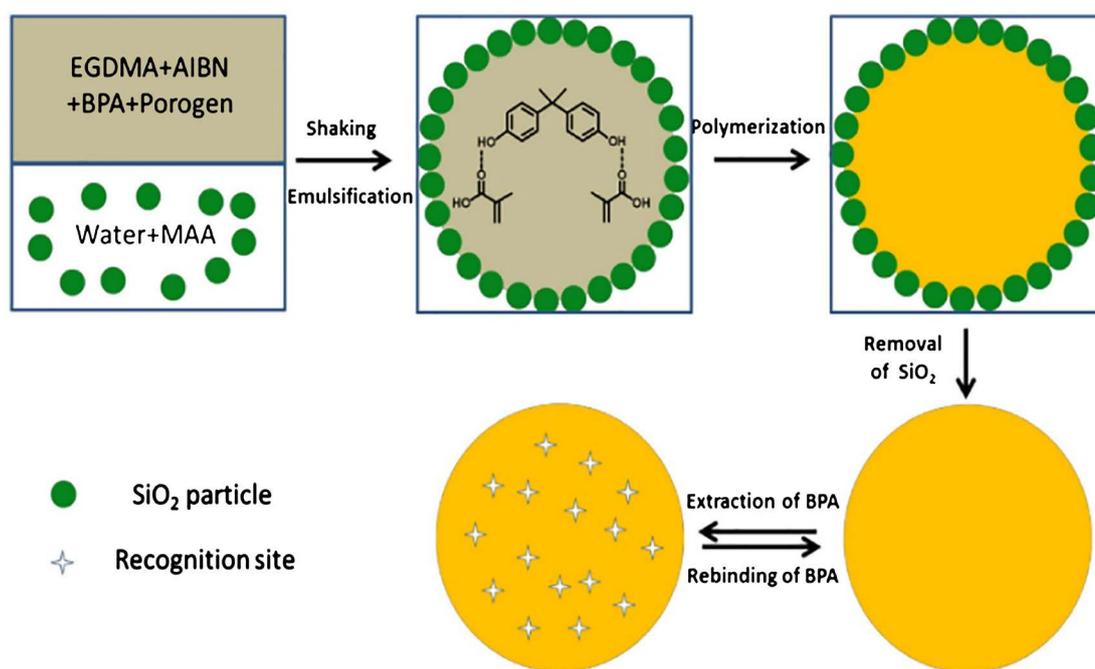
3.3. The Use of Interfacial Pickering Emulsion Polymerization to Enhance Water-Compatible

In order to reduce hydrophobicity thus reducing unselective binding of target pollutants, the interfacial Pickering emulsion technique which considers the immobilization of template molecules on the surface of MIP nanoparticles via oil-in water polymerization has recently gained attention in the synthesis of MIPs [72] [73]. Ye *et al.* were able to successfully develop interfacial MIP microspheres with well-controlled hierarchical structures when they employed template modified nanoparticles as stabilizers [72]. In the process of immobilizing molecular template on the surface of SiO₂ nanoparticles, the group made use of the interfacial molecular imprinting at which emulsion was subjected to

thermal polymerization. There was a formation of tiny indentation of binding sites and hydrophilic surface after the removal of template-modified silica nanoparticles from the MIP particles. In confirming the immobilization of the templates using ATR-FTIR, they had an excellent peak of 1530 cm^{-1} which corresponded to the C-H bending vibration as well as peaks of 2860 and 2956 cm^{-1} which respectively corresponded to the CH_2 symmetrical and unsymmetrical stretching. The modified SiO_2 also exhibited good selectivity in purely aqueous solution as juxtaposed to unmodified SiO_2 .

It has been observed that, both stability and compatibility of MIP microsphere is contingent on the amount of porogen (toluene) used, and the partitioning of MAA between the oil-liquid phase respectively [74]. Recently, Wang and co-workers with a maximum binding site number of $491\text{ }\mu\text{mol/g}$ were able to selectively detect bisphenol A using imprinted poly (methacrylic acid) microspheres with silica particles as a stabilizer via Pickering emulsion technique as shown in **Figure 7** [75]. The obtained microspheres after removing molecular templates and silica particles through post treatment from the surface of the spheres were observed to have regularly spherical structures (110 to $70\text{ }\mu\text{m}$,) and hydrophilic surfaces. The MIP microspheres showed high affinity and selectivity toward BPA in water.

Similarly, in synthesizing magnetic interface molecularly imprinted microspheres using super-paramagnetic behavior, Zhang *et al.* through photo-initiated Pickering emulsion polymerization and interface-imprinting technology were able to selectively recognize and separate template peptide in aqueous phase [76]. The synthesis process of MIMIMs at the aqueous phase was basically the



Ref. [75].

Figure 7. Schematic steps in the synthesis of MIP microspheres via Pickering emulsion polymerization.

immobilization of template on the surface of silica. After polymerization, silica nanoparticles were removed using $\text{NH}_4\cdot\text{HF}_2$ as an etching agent. It was then followed by a thorough washing using acetic acid and deionized water to remove IHH. The obtained results demonstrated an excellent selectivity and separation of MIMIMs toward peptide as a result of highly etched sites and magnetic susceptibility.

The use of Pickering emulsion polymerization in the production of water-compatible imprinted polymers does not only possess the quality of stability as compared to conventional organic surfactants but also improves template molecule mass transfer during templates removal and rebinding. The ability of fabricated MIP polymers to switch from organic solvent to water, using the technique of Pickering emulsion encompasses both the requirement of selectivity and detection of template in aqueous phase and this is considered as an advantage of Pickering emulsion polymerization [76] [77]. However, drawbacks when using Pickering emulsion polymerization may arise when polymerization temperature is increased: selectivity tends to decrease [78].

3.4. Use of Specially Designed Functional Monomers

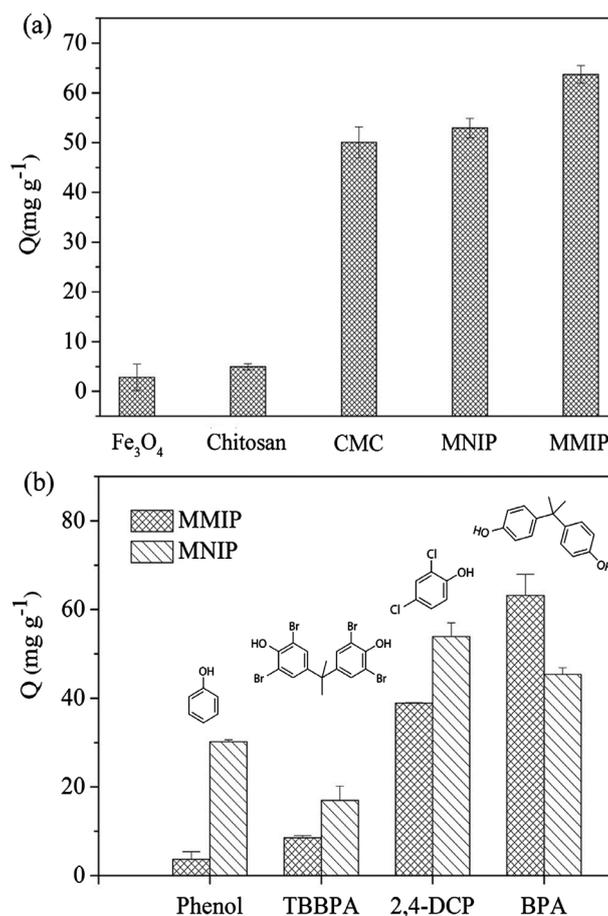
A remarkable technique that ensures the optimization and use of MIPs in pure aqueous environment is through specially synthesized functional monomers that easily allow the efficient formation of a template-functional monomer matrix. These specially devised functional monomers with their inherent ability to form a template-functional monomer matrix in aqueous media leads to the formation of MIPs with excellent recognition ability in aqueous solutions [79]. Several specially designed functional monomers worth noting are 1-(α -methyl acrylate)-3-methylimidazoliumbromide(1-MA-3MI-Br); 2-acrylamido-2-methyl-1-propane sulfonic; N, N'-diethyl(4-vinylphenyl) amidine; 1-(3,5-bis (trifluoromethyl)phenyl)-3-(4-vinylphenylurea); and the various forms of cyclodextrins (modified and unmodified cyclodextrins).

Luo and co-workers [80] via suspension polymerization were able to prepare caffeine-imprinted polymers using 1-(α -methyl acrylate)-3-methylimidazolium bromide (1-MA-3MI-Br) which had π - π and hydrogen-bonding interactions as a functional monomer. In order to compare the selectivity and adsorption capacity of 1-MA-3MI-Br-MIP toward caffeine, another MIP using MAA as functional monomer was prepared. Again, to know whether 1-MA-3MI-Br-MIP has an outstanding affinity toward caffeine in water, (theophylline was used as a control substrate), with three different solvents (methanol, acetonitrile, and methylene dichloride) being used to help draw inferences. The results obtained through adsorption isotherm experiments showed 1-MA-3MI-Br-MIP to have a maximum adsorption capacity of 53.80 $\mu\text{mol/g}$ as juxtaposed to MAA-MIP which had an adsorption capacity of 28.90 $\mu\text{mol/g}$.

The study also revealed 1-MA-3MI-Br-MIP to have the highest adsorption of caffeine in water as compared to methanol, acetonitrile, and methylene dichlo-

ride. The high performance of 1-MA-3MI-Br-MIP is suggestive of an existence of both hydrogen bond and hydrophobic interactions with caffeine unlike MAA-MIP which had a simple hydrogen interaction with caffeine. Again 1-MA-3MI-Br-MIP's good compatibility with water as compared to the other solvents was associated to the presence of the many imprinted cavities which were formed as a result of the hydrogen bonding interactions and charge transfer during polymerization.

The unique ability of cyclodextrin to form host-guest complexes with hydrophobic molecules and other substrates as a result of their structure makes them good choice materials in the synthesis of molecularly imprinted polymers. Recently, D. Huang *et al.* synthesized an MIP using Beta-cyclodextrin (β -CD) modified magnetic chitosan as functional monomer with MAA as assistant functional monomer (Figure 8) [81]. The combined properties of β -CD which is known to have a structure of hydrophobic inner cavity and hydrophilic exterior, and chitosan a hydrophilic biocompatible linear polysaccharide with abundant $-\text{NH}_2$ and $-\text{OH}$ improves the selectivity of β -cyclodextrin modified magnetic chitosan (β -CMC). In employing the FT-IR during characterization, it was observed that the absorption band of β -CMC was at 576 cm^{-1} owing to Fe-O bond



Ref. [81].

Figure 8. Adsorption comparison and selectivity of MMIP.

in β -CMC, compared with 540 cm^{-1} for MMIP and 541 cm^{-1} for MNIP that β -CD and chitosan onto the magnetic carriers ensured the excellent selectivity of β -CMC toward BPA from wastewater.

BPA's structural analogs which included dispersed phenol, TBBPA, and 2,4-DCP were selected as competitive templates when testing for the selectivity of β -CD-MMIP toward BPA: these selected templates were dispersed in a 100 mL conical flask. **Figure 8(b)** which is the result of the experimental analysis indicates β -CD-MMIP to show an outstanding selective affinity toward BPA as juxtaposed to the other templates. MNIP was seen not to have significant difference toward the adsorption of BPA and its analogs. Also, as observed in **Figure 8(a)**, β -CMC was observed to have better binding capacity with BPA as compared to nano- Fe_3O_4 and chitosan. The binding capacity of nano Fe_3O_4 was enhanced only after the introduction of $-\text{OH}$, $-\text{NH}_2$ and hydrophobic cavity on it. The MMIP only increased slightly as compared with β -CMC and MNIP which was a result of the thin imprinted layer. This indicates covalent modification played a significant role in enhancing adsorption performance.

In considering the selectivity of MMIP toward BPA, the study gave premium to the hydrogen bonds that existed between the imprinted cavities and BPA molecules as well hydrophobic interactions though the thin imprinted layers contributed to the selectivity of MMIP. The presence of $-\text{NH}_2$, $-\text{OH}$, the functional groups of carbonyl and carboxyl together with the modification of both β -CD and chitosan were largely the interactions which were possessed by the thin imprinted sites of MMIP.

3.5. The Use of Hydrophilic Functional Monomers or Co-Monomers

A representative approach through which MIPs synthesis to be used in aqueous media can be enhanced is using hydrophilic functional monomers. Commonly used hydrophilic functional monomers may include acrylamide [82], methacrylamide [83], and 2-hydroxyethyl methacrylate (HEMA) [84]., PETA, poly (ethylene glycol) diacrylate [85], N, N-methylene bisacrylamide [86] and N, N-ethylene bisacrylamide [87] are often used as hydrophilic cross-linkers. Employing this technique can produce outstanding performance of imprinted polymers designed to be used in aqueous solution by way of reducing non-specific binding while avoiding complicated post-surface modifications.

Duan and coworkers were able to synthesize a highly effective MIP toward the detection of bisphenol A (BPA) through RAFT polymerization in using 2-acrylamido-2-methylpropanesulfonic acid (AMPS) which is both polymerizable in organic and aqueous solution, [88]. In using either AMPS or 4-vinylpyridine (4-VP) as monomer, the molecularly imprinted polymers were synthesized on carbon microspheres under room temperature. In performing the adsorption test, it was observed that AMPS/MIPs had an outstanding adsorption and excellent affinity for BPA with a binding capacity of 5.38 mg/g as juxtaposed to 4-VP/MIPs. This observation and high performance of AMPS/MIPs was attri-

buted to AMPS/MIPs dispersion ability in water. This ensured that BPA molecules were able to adequately access imprinted cavities hence an improved adsorption characteristic.

Elsewhere, Wang and coworkers synthesized a water-compatible imprinted polymer that is thermos-sensitive in nature, using acrylamide (AAm) and 2-acrylamide-2-methyl propanesulfonic acid (AMPS) as functional monomers through precipitation polymerization [89]. The MINP which exhibited a zipper-like switchable interaction between poly (AAm) and poly (AMPS) was shown to have an excellent molecular recognition ability and selectivity toward Levofloxacin (LOFL). The static absorption experiments revealed AAm and AMPS to exhibit an excellent thermo-responsive and a high molecular recognition and selectivity ability toward Levofloxacin. The electrostatic interaction between sulfonic group of AMPS and tertiary amine of LOFL had a bearing with the high affinity of the prepared MINP toward LOFL.

In another work, as shown in **Figure 9**, Duan *et al.* in using 2-acrylamido-2-methylpropanesulfonic acid (AMPS) and styrene (St) as bi-monomers and porous graphene oxide (PGO) as a support-matrix synthesized a highly effective MIPs toward the detection of bisphenol A (BPA) through RAFT polymerization [90]. In a competitive adsorption test of BPA; tetrabromobisphenol A (TBBPA);

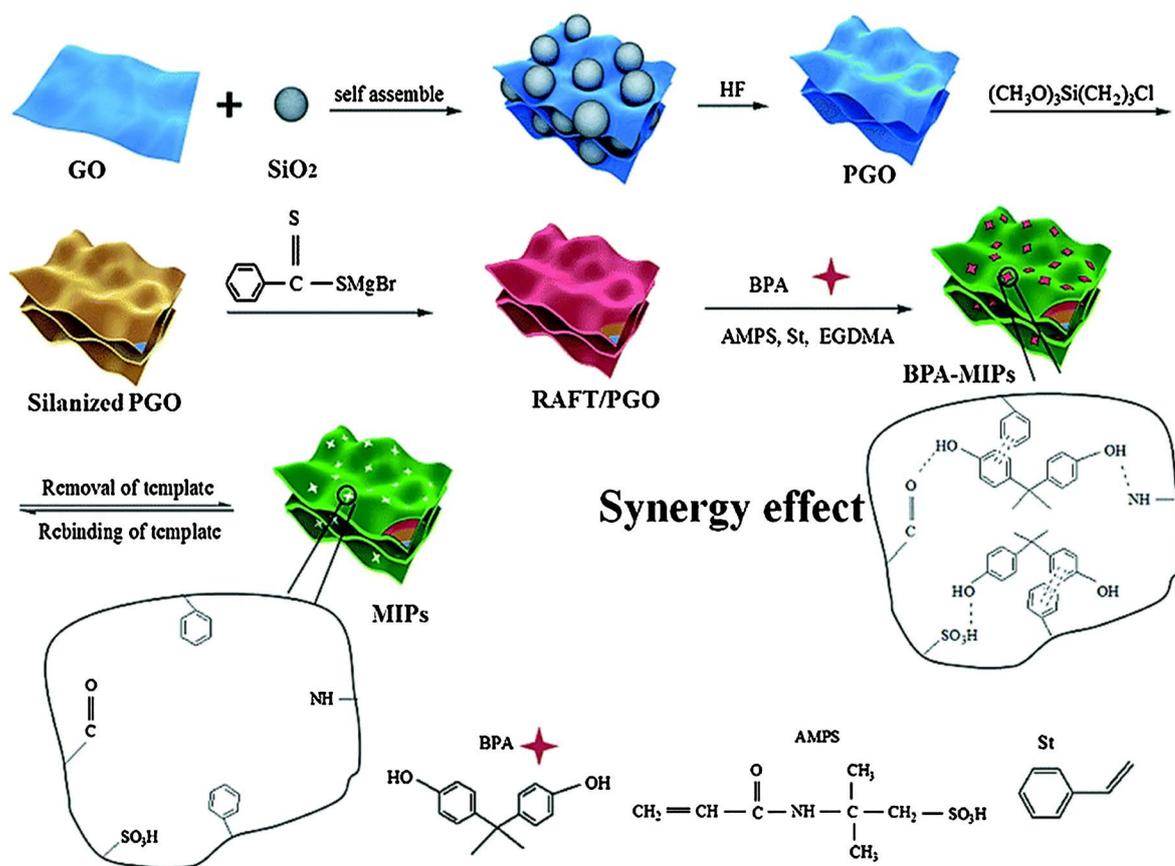


Figure 9. Schematic procedure of MIP preparation.

and 4-*tert*-butylphenol (BP), The study revealed that, the synergistic nature of AMPS and St, enhanced the adsorption selectivity and stability of the prepared AMPS-St/MIPs up to 85.7 mg·g⁻¹ at 293 K in the BPA's adsorption in aqueous media as compared to PGO and AMPS-St/NIPs which had adsorption capacity of 66.3 mg·g⁻¹ and 40.9 mg·g⁻¹ respectively. This observation and high performance of AMPS-St/MIPs was attributed to AMPS hydrophilic dispersion ability in water and St' stable π - π stacking interactions with BPA. Formation of hydrogen bond between AMPS and template BPA enhanced water compatibility as well as reduced nonspecific adsorption of AMPS-St/MIPs. More so, the porous structure and high surface area of PGO which served as a support for AMPS-St/MIPs increased the specific incorporation of BPA analytes. All discoveries illustrated that, the combination of AMPS and St enhances performance and adsorption properties of MIPs synthesized to work in water.

4. Challenges in Using MIPs for Water Treatment

Over the last decade, molecular imprinting technique has been developed and adopted both from a material point of view and from an application point of view for various analytical and treatment purposes. However, there seems to be some challenges chemist or material scientist face with respect to imprinted polymers' compatibility with water: these challenges need to be studied and addressed.

Leaching of residual template from imprinted polymer remains a formidable challenge especially in analytical application like MISPE, and largely leads to quantification inaccuracies [91] [92]. To overcome this challenge and avoid interferences, template has been removed using pressurized hot water extraction [93]; using analogue of target molecule as template [94], and the use of other accelerated solvent extraction. Surface imprinting has also been employed as a means through which recognition sites are localized on the surface of suitable substrate [95]. These techniques have had impressive extraction efficiencies yet there exist challenges such as slow adaptation of solvent, reduced selectivity toward analyte, and remnants of template trapped in cross-linked domain of the polymer structure.

Although guided efforts by researchers and scientist to fabricate water-compatible MIPs either by the introduction of hydrophilic properties into the imprinted polymer or modification of binding solvents have achieved considerable success, there is however a need to do more. MIPs prepared by these approaches may have challenges of uneven swelling, heterogeneous binding sites and may invariably lead to nonselective binding. It is therefore imperative to improve the synthesis approach in order to obtain MIPs with specific and homogeneous population of binding sites. This can be done by way of searching for more hydrogel layers and novel formats in the design of special hydrophilic monomers.

Comprehensive studies and literature that present potential health effects and

toxicity of MIPs in water treatment are considered insufficient [96]. This may raise questions of how feasible and safe it is to employ MIPs in the treatment of water on commercial basis. To achieve full confidence of potential users of MIPs in water purification, it is recommended a lot of research and careful studies on potential health effects of MIP be taken.

5. Conclusion

This review presented MIP as a novel material which has the potential to be used as selective sorbent to clean up pollutants in water. The information in this study underscores some critical parameters and the various synthesis approaches on how to synthesize MIPs that are compatible with water. Despite the tremendous progress in the field of molecular imprinting, one challenging task most contemporary chemist faces is the fabrication of imprinted polymers that have high recognition and adsorption ability in aqueous solution. Using strategies such as surface post-modification, specially designed functional monomers, interfacial Pickering emulsion polymerization, and hydrophilic functional monomers or co-monomers, the challenge of nonspecific selectivity and adsorption of MIPs was seen to have been reduced. We anticipate further improvements and myriad of studies which will not focus only on the development of selective adsorption but also enhanced sensitivity and detection of components that pollute water.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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