Molecularly Imprinted Nanotechnology: Core Shell and Carbon Dots based Imprinted Polymers

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Abstract

Molecularly imprinted technology (MIT) is able to mitigate natural biological receptors such as antibodies. The combination of MIT with nanotechnology results in the molecularly imprinted nanotechnology which exhibits enhanced selectivity and sensitivity. A new class of molecularly imprinted technology known as core shell imprinting polymerization offers greater benefits than bulk polymerization, such as easier template removal, increased yield, homogenous binding sites, uniform morphology, and a high mass transfer rate. Carbon dots (CDs) based MIPs have garnered the most attention of all the core shell-based MIPs because of their high fluorescence intensity, low cost, non-toxicity, biocompatibility from CDs, and high selectivity from MIPs. This work addresses the synthesis of core shell molecularly imprinted nanotechnology. Moreover, it addresses CD synthesis, passivation, and application. Subsequently, MIPs based on CDs are applied to detect various analyte molecules. Finally, the work's conclusion emphasizes the importance of CD-based MIPs and core shells for environmental applications.

Keywords: *Molecularly imprinted polymer; nanotechnology; core shell imprinting polymerization; selectivity; carbon dots; sensing*

Highlights

- Molecularly imprinted polymers as artificial receptors.
- Molecularly imprinted nanotechnology improves selectivity and sensitivity.
- Core shell-based MIPs proves better than bulk MIPs.
- Carbon dots-based MIPs offers luminescent properties and selectivity.

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1. Introduction

The recognition process found in nature is very specific and has fascinated scientists and researchers. Molecular recognition represents the basis of most structures and functions involved in biological fields. The life processes involve very sensitive and specific interactions on molecular level e.g. antibody-antigen interactions, enzyme-substrate interaction and replication, transcription, and translation process of DNA. The specific recognition properties of the above systems found in nature have attracted many researchers for the design of synthetic materials that have specific recognition properties. Molecular imprinting involves the creation of synthetic receptors with specific recognition properties [1]. The specific recognition by molecular receptors can occur via the formation of non-covalent bonds or covalent bonds. However, in biological systems mainly non-covalent interactions are involved in such recognitions. Molecular imprinting is a technique which is used for the creation of artificial receptors which have specific recognition abilities as in natural systems [2]. Such artificial receptors may also possess certain advantages over natural receptors such as antibodies. The synthesis of artificial recognition systems does have advantages over antibodies. While antibodies are used in a wide variety of analytical applications, they are costly and have a comparatively short shelf life. The aim of molecular imprinting is to generate synthetic receptors containing specific receptor sites capable of binding to selective template molecules as in case of natural receptors. There is always a need for more sensitive and selective analytical procedures particularly for the pharmaceutical industries, environmental industries and in biomedical analysis. As a result of large number of analytes development of fast methods is required. One of the most promising and potential areas of analytical endeavour is that of molecular imprinting. Molecular Imprinting Technology (MIT) [3] which involves design of specific molecular recognition substances capable of imitating natural recognition sites is considered as one of the most efficient and versatile tools capable of recognising both biological and chemical molecules including amino acids and proteins [4-6], derivatives of nucleotide [7], pollutants [8, 9], drugs, and food [10, 11]. Molecularly Imprinted Polymers (MIPs) have gained importance as chemical agents of high sensitivity and affinity, which are of considerable use in sensor development [12]. They also have many other applications such as in separation sciences and purification [3-18], catalysis [19], delivery of drugs [20], biological receptors, and antibodies [4, 21, 22] in environmental analysis.

The process of molecular imprinting involves the organization of polymerizable monomer molecules around a template or imprint molecule, followed by the polymerization in the presence of a cross-linker. The monomer should contain complimentary functionalities with

respect to the template molecule. In the presence of cross-linking agent, a three-dimensional polymer network is formed. As the process of polymerisation is completed, the template is removed from the three-dimensional polymer which leaves the specific binding and recognition sites which are complementary to size, shape and functional group moieties of template [23]. A schematic representation of molecular imprinting is shown in Figure 1. There must be good interaction between analyte and monomer to obtain molecularly imprinted polymer (MIP) networks with specific recognition site. There are mainly two approaches to obtain molecularly imprinted polymers. Firstly, there is self-assembly [24] approach, which uses non-covalent forces such as hydrogen bonds, van-der Waal forces, ion or hydrophobic interactions, and metal coordination. Secondly, there is the covalent, or pre-organised approach [25] which employs reversible covalent bonds, usually, involving a prior chemical synthesis step to link the monomers to the template. It is generally perceived that non-covalent imprinting leads to formation of more flexible polymers which can be used for a range of targets and is easier practically while covalent imprinting yields better-defined and more homogenous binding sites. However, removal of template from the polymer is difficult in case of covalent or pre-organised polymers as it will require cleavage of bond. Among these, self-assembly is the most widely used approach for the synthesis of MIPs due to its simplicity and ease to remove the template. Another synthetic protocol for obtaining MIPs is semi-covalent approach [26]. It combines the advantages of both covalent and non-covalent approaches. The interactions between the template and monomer are very important which derive the molecular recognition phenomena. Thus, the resultant polymer recognizes specifically and binds the template molecule. The main advantages of MIPs are their high selectivity and affinity for the target molecule used in the imprinting procedure [27]. Moreover, imprinted polymers have higher strength, robustness, resistance to elevated temperature and pressure, and inertness towards acids, bases, metal ions and organic solvents as compared to biological systems. In addition, their synthesis is less expensive and the storage life of the polymers is high, sometimes maintaining their recognition capacity for several years at room temperature [3].

2. Molecular Imprinting Nanotechnology

MIT is a very useful method to serve the purpose of molecular recognition. When MIT is combined with nanotechnology, molecularly imprinted nanomaterial is obtained which exhibit enhanced sensitivity and selectivity, due to the combination of both technologies, which result in the development of more suitable matrices for desired applications [28]. A large number of imprinted nanomaterials have already been formed, such as imprinted nanoparticles [29], imprinted nano-composites [30], and imprinted hybrid materials [31] for a wide application, such as separation science [32], molecular recognition [33], and chemical sensing of different analytes [34]. Imprinted nanomaterial has gained much importance, due to their foremost advantages, such as high surface area, large number of predetermined recognition sites, high chemical and thermal stability, comparative simplicity, low preparation cost, and potential application to a variety of analytes [35, 36]. The ease of formation of imprinted nanomaterial and straightforward compliance also play a vital role in achieving greater success as compared to other receptors [37]. Imprinted materials with nanoscale dimensions have significantly contributed to various fields of application of imprinted materials such as sensors, selective adsorption and separation, drug delivery, solid-phase extraction, catalysis,

environmental analysis, and other fields and can potentially have a greater impact on nanoscience and technology in the future.

The nature of bonding interactions and the compatibility between the template and monomers in a typical polymer matrix plays an important role. The most widely used protocol for synthesis of MIPs is bulk polymerisation [38]. It imprints the molecule on polymer by bulk polymerisation. In bulk polymerisation, functional monomer prearranges around the template in presence of organic solvent and then copolymerise in presence of cross linker and initiator. The resulting polymer is then crushed and sieved to obtain particles. After the template molecules are removed specific recognition sites complementary to template are obtained. But this technique has many limitations such as time consuming and complicated preparation process and less recognition sites that lead to poor binding capacity of template molecule in a polymer matrix [39]. To increase the efficiency and recognition of MIP towards template molecules, MIP nanoparticles having large surface to volume ratio have been prepared. Thus, imprinting cavities are more accessible to template molecules which also show improved binding kinetics. Many methods have been developed for the formation of MIP nanoparticles, the most popular synthetic strategies being precipitation polymerisation, emulsion polymerisation, template synthesis approach, core shell polymerisation. The precipitation polymerisation involves the formation of molecularly imprinted nanoparticles in excess of solvent. The polymerisation process results in formation of polymers insoluble in solvent which precipitate out from the reaction medium. Monodispersed molecularly imprinted nanoparticles first synthesized for β-estradiol and theophylline by precipitation polymerisation [40]. Precipitation polymerisation has been used for the production of molecularly imprinted nanoparticles from the last two decades. The process is less time consuming and easy. By optimizing the amount of monomer, cross linker and template uniform nanoparticles with improved binding characteristics can be obtained [41]. However, the use of excess solvent is one of its limitations which have a negative effect on the bonding of template and monomer. Emulsion polymerisation involves the mixture of cross linker, functional monomer with the template in an aqueous phase and their emulsification by adding surfactant with vigorous stirring or ultra-sonication. Co-stabilizer e.g. sodium dodecyl sulphate (SDS) is added to the disperse phase which suppresses the diffusion process in continuous phase. This results in the formation of stable emulsions of homogenous uniform particle size, this is called mini emulsion polymerisation [42]. Another approach for emulsion polymerisation is micro emulsion polymerisation which takes place in a dispersion made of water, oil, and surfactant [10]. The mini emulsion polymerisation method was applied to synthesize semi-covalent MIP nanoparticles for the imprinting of glucopyranoside [26]. In template synthesis approach, porous support membranes are introduced to form surface imprinted nanoparticles in their pores. Such MIP nanoparticles embedded in support material can be applied for membrane separation [43, 44]. By varying different high viscosity polymerisation solvents, particles of controlled nano-sizes can be synthesized. High surface areas MIP nanoparticles can be obtained by using the support material. However, so far only few MIP nanoparticles have been synthesized by template synthesis approach [45, 46].Core shell polymerisation [47] involves synthesis of imprinted polymers as a shell around a core.

3. Core Shell Polymerisation

Core shell polymerisation combines the material properties of MIPs and core shell to give high functionalized materials. Both materials have their own unique properties such as large surface area, high specificity and sensitivity, which combine to give materials which have specific characteristics of both [48]. Many materials have been used as core shells in polymerisation as shown in Figure 2. Normally cores are synthesised according to the characteristics of template and functional monomer. The core materials which are generally used include silica, magnetic nanoparticles, semiconductor quantum dots (SQDs), Ag and Au nanoclusters etc. Silica is an inorganic inert material which has been widely used due to its different properties such as stability under acidic conditions, thermo-stability, good biocompatibility, excellent permeability to the template molecules. One of the best methods to prepare silica nanoparticles is by Stober Method [49]. It involves the hydrolysis of tetraethylorthosilicate in basic conditions. Vinyl groups are mostly used to modify silica cores. Many silanes amino groups such as 3-aminopropyltriethoxysilane (APTES), N-β-(aminoethyl)-γ-aminopropylmethyldimethoxysilane (AEAPMS) are also used to modify silica cores [50]. Due to chemical inertness of silica, it doesn't affect the properties of polymer. Thus, it is suitable material to be used as core. Magnetic nanoparticles possess magnetism. Iron, cobalt, nickel and their oxidizing agents or alloys have been used as core shell [51]. But Co and Ni have limitations in biological and pharmaceutical field due to their toxicity. However, iron oxide (Fe_3O_4) has proved as better core shell material due to its low toxicity, low cost, and ease of preparation [52]. SQDs are kind of nanoparticles composed by II-VI group elements having particle sizes between 1 to 10 nm [53]. SQDs can be synthesised in organic or water phase. However organic phase is beneficial for SQDs with high dispersion and uniform size distribution [54]. SQDs synthesized in organic solvents have hydrophobic surface which can't be used in biological systems. SQDs prepared in water are stable, have good solubility and can be used in biological systems directly. They have many optical and electrical properties; have high fluorescence intensity broad absorption bands with sharp emission [41]. Due to these properties, SQDs combined with MIPs are highly applicable as sensors [55]. Ag and Au nanoclusters have also been used as cores for core shell materials [56].

Modification of nanoparticles surface with proper organic or inorganic material is needed to ensure stability of nanoclusters and provide more functionality for specific recognition properties. Modification of cores by some functionalizing reagent also improves their efficiency towards polymerisation. Modified cores have better stability and biocompatibility and higher surface area [57]. Core shell MIPs have been prepared by surface imprinting technique [58]. Large numbers of surface imprinting sites are formed at the surface of substrate which are easily accessible with favourable binding kinetics. Template/ monomer interactions are not diffusion limited to the same extent as was problem encountered in bulk imprinting [59]. Core shells MIPs have wide applications. Their main applications till now have been in solid phase extraction and development of sensors [60]. Among the various core materials, mainly silica cores and magnetic cores are used in solid phase extraction whereas SQDs and carbon dots are used for sensors. Core shell MIPs may overcome many limitations of bulk MIPs (Table 1).

4. Synthesis of Core Shell MIPs

Core shell MIPs are mostly prepared by surface imprinting technique [58]. High surface imprinting sites are formed at the surface of substrate which are easily accessible with favourable binding kinetics. Template/ monomer interactions are not diffusion limited to the same extent as was problem encountered in bulk imprinting [61-63]. In surface imprinting technique, less amount of template is used because template used only in surface coating step. Surface imprinted polymers have been used for different type of analytes. Several methods have been used for surface imprinting. Some of the important methods are listed below:

4.1. Soft Lithography

It is one of the most useful techniques used for the synthesis of sensors by surface imprinting. This technique was first used by Bain and Whitesides in 1989 [64]. In this technique, micro and nano scale patterns are formed on the solid substrates. A pre-polymerised layer is formed on the surface of substrate and after a certain period of time template stamp is pressed over the surface. Self-assembling of the template structures on to smooth support are used to produce template stamp which are complementary to shape, size and chemical functionality of template. Usually, glass slide is used for the solid support due to its rigidity. Due to this technique highly specific and sensitive recognition sites are formed on the surface.

4.2. Emulsion Polymerisation

It is the most direct technique for producing core shell MIPs. It involves a two-stage process: production of mono dispersed seed latex and creation of an imprinted shell using emulsion polymerisation [65]. However, the presence of surfactants represents serious drawback for standardizing the complex procedure both in terms of particle dimension and imprinting effects. This technique displayed high specific recognition sites and has potential to be used for the preparation of highly selective biosensor surfaces in further applications.

4.3. Grafting Polymerisation

It is another method for preparing core shell nanoparticles. It involves grafting a thin layer of MIPs on to the surface of prefabricated nanoparticles [66]. It can be done by two approaches: grafting to and grafting from. ‘Grafting to’ is a kind of covalent reaction between different functional groups and grafting polymer brushes will be grafted on core and final functionalized cores are synthesised. ‘Grafting from’ includes an initiation reaction. Functional groups on the core would initiate polymerisation reaction of functional monomers [67].

4.4.Sol Gel Polymerisation

Sol gel technique is a process to develop inorganic polymer materials wherein molecular precursors dissolved in liquid are first hydrolysed to form solid in liquid dispersion (sol) immediately followed by their condensation to provide a solid network filled with liquid (gel) [68]. Sol gel process involves mainly five steps: sol formation, gelation, aging, drying, and densification. It involves precursors which are necessary for sol process. Precursors can be inorganic salts or organometallic compounds which are stable and soluble in liquid being used as solvent (Figure 5). Predominantly metal alkoxides are used as precursors [69]. The solvents used include both protic as well as aprotic, depending upon the nature of precursor. Solvents such as DMSO, alcohols, ketones and amines are generally used. Hydrolysis occurs by the addition of water in the presence of acidic, basic or neutral conditions. An SN_2 reaction occurs in the presence of acid which leads to the formation of silanol moiety. This is followed by the poly-condensation step which aggregates silanol moieties altogether to form tons of siloxane

linkages. Finally, a sol is formed from these siloxane particles. This two-phase system contains amorphous particles and liquid phase is irreversibly formed from a single-phase liquid system. This is followed by aging to enlarge the cross-linking degree in the system and then the liquid phase is removed from the pores of amorphous particles resulting in sol gel shrinking followed by pores disintegration which keeps the sol gel to be denser. Sol-gel process is one of the efficient methods for polymerisation as compared to other methods because of its simplicity and ease of preparation. Polymerisation occurs after the hydrolysis step with connectivity spanning throughout the solvent which leads to the development of wet gel which strengthens by using controlled thermal process, one of the major advantages is that it needs no extreme temperature for polymerisation. The porosity and pore size can also be varied by changing the precursors. It shows better homogeneity and purity, minimize the evaporation loses and air pollution. Thus sol-gel process is one of the versatile methods for the formation of polymer matrix in core shell polymerisation [70].

4. **Carbon Dots as core in core shell MIPs**

In recent years, fluorescent nanomaterial has attracted keen interest of various researchers because of quantum size effect and high fluorescence intensity. These fluorescent nanomaterials overcome the shortcomings of traditional fluorescent dye probes like low stability, less solubility, and weak fluorescence intensity and can be used in various chemical, physical and other related fields [71]. Of all the fluorescent nanomaterial, SQDs have proved best in many applications due to their unique electrical, optical and luminescent properties [72-74]. However, most of the SQDs contain heavy metals which limit their applications due to their toxicity [75-77]. Therefore, the development of new nontoxic heavy metal fluorescent nanomaterial has been the current trend. Carbon dots (CDs) are new class of fluorescent nanomaterial which show unique optical, electronic and luminescent properties. CDs are mainly composed of carbon element and possess chemical inertness. They have proved better than quantum dots due to their low toxicity, low molecular weight, high hydrophilicity and eco-friendly nature [78].

5.1. **Synthesis of Carbon Dots**

There are many sources for the synthesis of carbon dots. Carbon dots were accidently discovered in 2004 by Xu *et.al.* [74] as a by-product of electric discharge of carbon nanotubes by gel electrophoresis. Since then, carbon nanomaterial has attracted much interest as a new class of fluorescent materials and led to research for the specific synthesis of carbon nanomaterial, which were later termed as carbon quantum dots. In 2006, Sun *et.al.* [79] synthesized carbon dots for the first time by the laser ablation of graphite powder/cement mixture at high temperature. The synthesised carbon nanomaterial had diameter less than 10 nm and thus termed as carbon dots (CDs). In the recent decade, there has been much progress in the synthesis of carbon dots [80]. There are two main approaches for the synthesis of carbon dots: top-down approach and bottom-up approach. Top-down preparation of fluorescent carbon dots are the early approaches which include arc discharge method [74, 79-81], electrochemical oxidation [82-85], and laser ablation method [86-88]. Bottom-up approaches are based on the polymerisation of small molecules to the nanoscale carbon dots. They include hydrothermal method [89-93], microwave assisted pyrolysis method [82, 94-96], ultrasonic method [97], acid dehydration method [95], and pyrolysis method [98, 99] Among these, hydrothermal method

and microwave assisted pyrolysis method are most widely used which can be realised by one step method for preparing fluorescent CDs.

5.2. Surface Functionalization of Carbon Dots

Surface functionalization or passivation is necessary to make the CDs fluorescent. Unmodified CDs shows weak fluorescence, so modification by functionalizing reagent is a necessity. This creates a fundamental difference between CDs and other photo luminescent materials especially quantum dots. In quantum dots, the fluorescence occurs due to the quantum effect of nanoscale particles between energy levels allowing excitation of electrons from valence band to conduction band in discrete energies. In contrast, the fluorescent properties of CDs are associated with surface defects responsible for absorption of light in different wavelengths i.e different colors. Thus, passivation of CDs plays a central field in photo luminescent properties of CDs. Passivation can be done by many molecules such as with hydrocarbon chain like polyethylene glycol (PEG) [100]. Y.P Sun and colleagues passivated the CDs with polymers such as propionylethylenimine-co-ethylenimine (PPEI-EI) [101]. Many silanes functionalizing reagents were also used for surface passivation of CDs. Surface passivation not only make CDs fluorescent but also play vital role in proliferation of carbon dots. It makes them hydrophilic-water soluble and thus make it available for many biological applications particularly biomedicines. There exists a large number of -OH, -COOH, -NH_2 groups on CDs surfaces which endow CDs with good solubility and binding capacity with various organic, inorganic or biologically active compounds as shown in Figure 3. CDs show strong absorption in the ultraviolet region which also extends to visible region [102]. By passivation of CDs, it gradually moves to red shift. The luminescent properties are electrochemical luminescence and photoluminescence, of which the prominent one is photoluminescence. The excellent properties of CDs include emission wavelengths, high fluorescence stability, tunable excitation, and nonblinking.

5.3. Applications of Carbon Dots

Due to their low toxicity, high fluorescence stability and small size, they have wide applications in the physical, chemical and biological fields as shown in Figure 3. The nanomaterials of high stability and absorption in visible region are of great interest in solving energy issues and environmental problems. Due to their excellent properties, these CDs are used as LED devices. CDs are also used in chemical sensing and are broadly used in metal ion detection, anion detection, small organic molecules and biomolecules detection. CDs are fluorescent probes which shows high fluorescence intensity however their intensity quench easily by metal ions due to electron accepting nature of ions in solution and also determine the concentration range at a certain level of metal ion in solution. Researchers had extended the CDs for the detection of anions and small molecules. Unlike, metal ions which quench the fluorescence intensity of CDs, anions and small molecules restore the quenching of CDs fluorescence and can be detected. Zong *et.al*. used spherical mesoporous silica as nanoreactor, added it to the solution of citric acid and other three inorganic salts and then ultrasonicated them to obtain CDs [95]. It was found that Cu^{2+} quench the fluorescence of CDs while on addition of L-cysteine to the solution, Cu^{2+} released from the surface of CDs to restore the fluorescence of CDs and thus detect L-cysteine in solution. Bai and other workers reported a sensor for detection DNA based on CDs. It was observed that methylene blue can effectively

quench the fluorescence of CDs, however in the presence of DNA in solution, the fluorescence of CDs was restored [99]. Xu *et.al.* reported aptamer functionalized CDs for protein detection [100]. This sensor showed high sensitivity and specificity towards thrombin. Due to low toxicity and high stability, fluorescent CDs proved better than SQDs. So, they can replace SQDs in bioimaging [101]. Sun and his co-workers applied fluorescent CDs in bioimaging [82]. They cultured MCF-7 cells vaccination in medium which contained CDs for 2 hours, the fluorescence area was observed to be mainly concentrated in cell membrane and cytoplasm by fluorescent microscope. Wang *et.al.* used vitamin B as carbon source and synthesized CDs by hydrothermal method which were applied to U-87 cell imaging [102]. The U-87 cells were cultured in medium containing CDs for 2 hours and found that only cell membrane and cytoplasm emit bright light fluorescence. Fluorescent CDs were also used for drug delivery due to their low toxicity and high stability. Lai *et.al.* synthesized CDs using glycerol as carbon source and PEG as passivator and using mesoporous silica nanoparticles to obtain uniform CDs. These were used as carrier for an anticancer drug doxorubicin [103].

5. Sensing application of carbon dots-based core shell MIPs

Fluorescent CDs, a fascinating class of carbon quantum dots, have attracted increasing attention in recent years and they can be used as an alternative approach for formation of cores in MIPs. The CDs are superior to quantum dots and fluorescent dyes due to their low cost, ease of synthesis, chemical inertness, good biocompatibility and low toxicity as compared to heavy metals commonly used in quantum dot cores [104]. The ease of functionalization of CDs is another advantage and various functional groups can be grafted onto the surface of CDs which affect both the optical and the physio-chemical properties of these nanoparticles. It has many wide applications. There is a lot of CDs combination however CDs linked with MIP is limited. Many researchers mainly focus on one carbon source for the preparation of CDs is citric acid and can be prepared by different methods. CDs coupled with molecular imprinting technique, in which CDs acts as core material and imprinted polymer layer around it to make it specific for the particular template (Table 2). In 2012, Y. Mao *et.al.* synthesized a novel and eco-friendly molecular imprinted polymer through one pot synthesis at room temperature by sol-gel polymerisation and applied it for molecular recognition element to develop dopamine fluorescent probe sensor [105]. This CDs-MIP fluorescent sensor was then applied for the selective and specific determination of dopamine in biological fluids such as human urine samples. It showed a linear relation between dopamine concentration and fluorescence response from 25-500 nM with correlation coefficient of 0.999 and detection limit was estimated to be 1.7 nM. In 2015, L. Feng *et.al.* developed a new method for the specific recognition of α-amanitin using CDs embedded in polymer matrix [97]. The detection limit of the method was found to be 15 ng mL^{-1}. G. Liu et.al. described an eco-friendly method for the recognition of bisphenol A [106]. They developed CDs encapsulated by molecular imprinted polymer for the fluorescent detection of bisphenol A. It was observed that fluorescence intensity decreases as the concentration of bisphenol A increases and also found a linear relationship between concentration and fluorescence intensity and the detection limit was found to be 30 nM. L. Xu *et.al.* prepared novel sensitive fluorescent sensor for the determination of sterigmatocystin in grains based on CDs embedded in MIP which was prepared by one pot reaction [107]. T. Hao *et.al.* reported facile and efficient method for the specific recognition of 4-nitrophenol by fluorescent amino modified CDs-MIP [108]. J. Hou *et.al.* developed an eco-

friendly and facile fluorescence sensor for the detection of tetracycline in milk by grafting MIP around CDs [109]. A linear response between fluorescence intensity and tetracycline concentration in the range of 20 nM to 14 µM was observed and detection limit was found to be 5.48 nM. R. Jalili and M. Amjadi developed a facile and novel sensor for the specific recognition of nifedipine based on silane functionalised CDs and imprinted polymer was synthesized by sol gel process. This sensor was used for the detection of nifedipine in serum and urine samples [110].

7. Conclusions

This study provides a thorough overview of the significance of combining nanotechnology and MIPs to create molecularly imprinted technology. Many of the drawbacks of conventional MIPs, including their high binding affinity, uniform binding sites, and low mass transfer resistance, have been addressed using core shell imprinted technology. Compared to quantum dots-based MIPs, CDs-based MIPs have many advantages due to their low cost of synthesis and absence of toxicity. For a wide range of analytes, MIPs based on CDs offer exceptional selectivity and sensitivity. In summary, MIPs based on core shells, including CDs based MIPs, offer an improved foundation for novel sensing materials in environmental applications.

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Figures

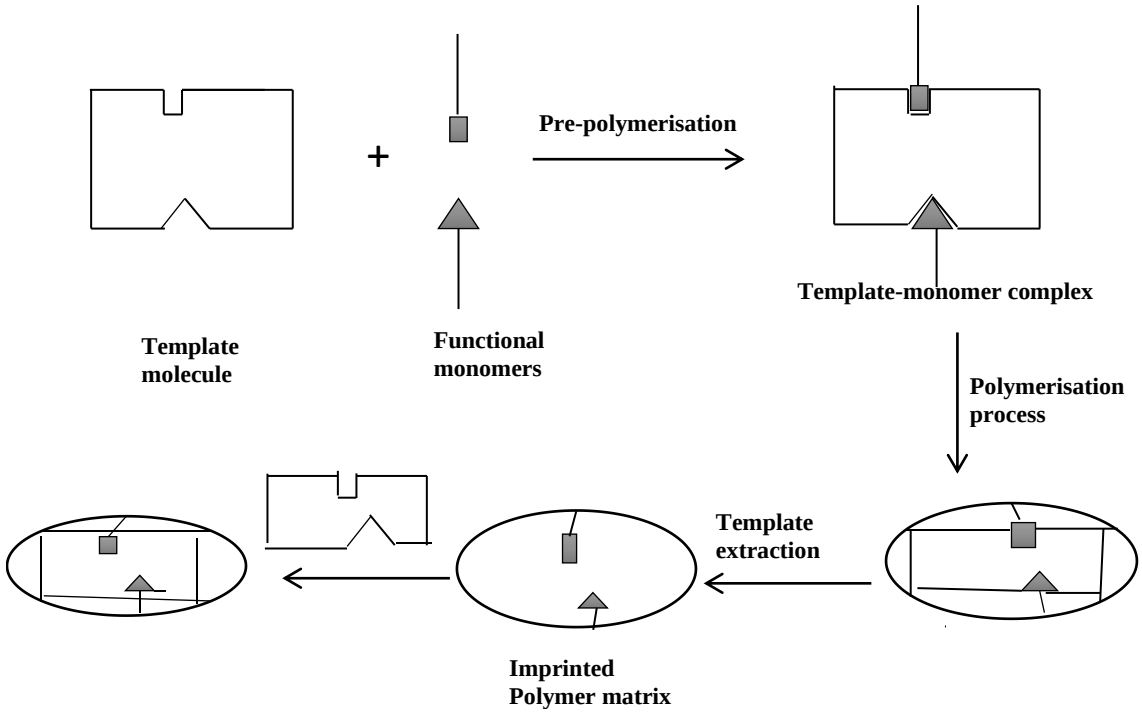

Figure 1. Schematic representation of Molecular Imprinting Process.

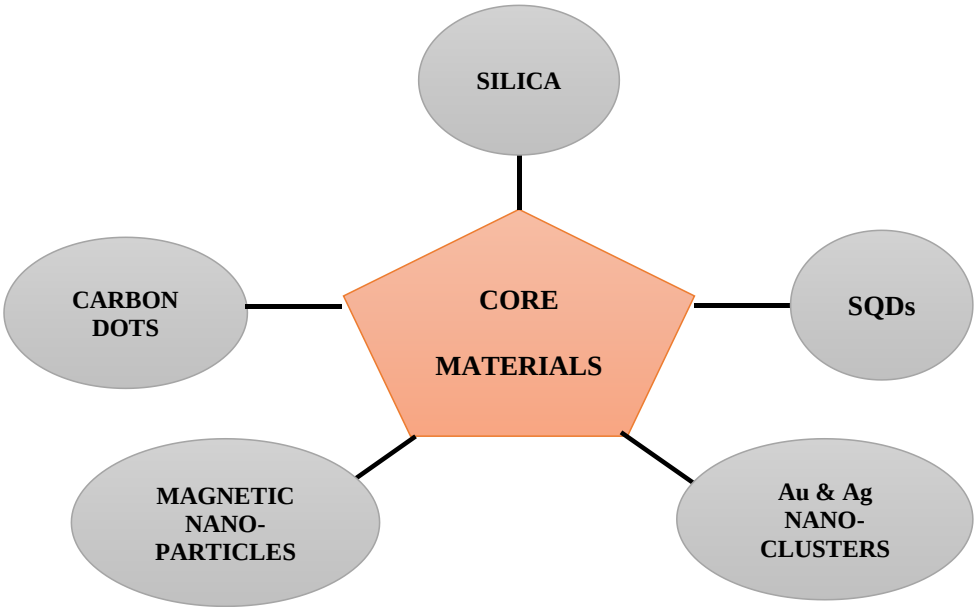

Figure 2. Core materials used in core shell MIPs

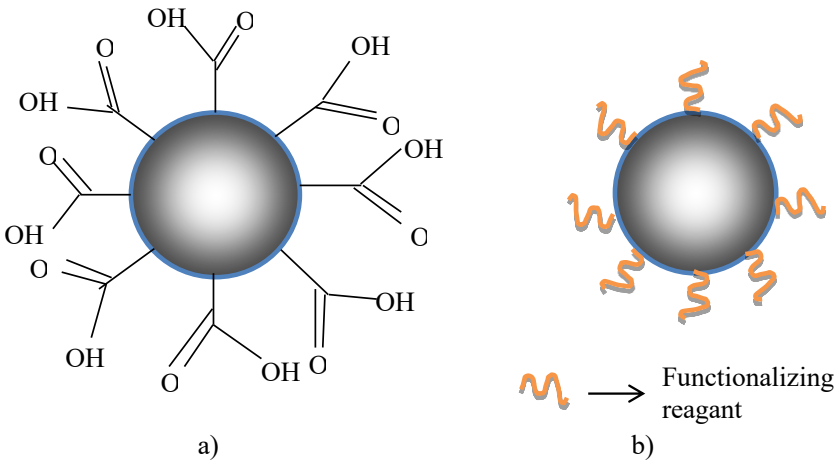

Figure 3: Passivation of carbon dots: a) Unmodified CDs b) Modified CDs

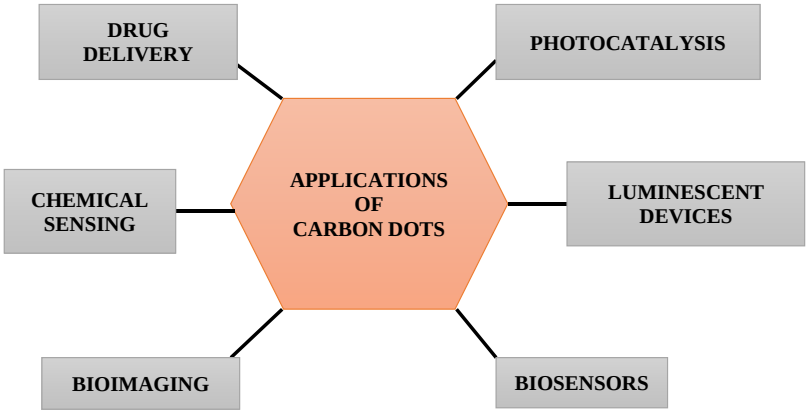

Figure 4: Applications of Carbon Dots

Sol gel Process

Organo-inorganic precursors:

Metal alkoxides

Metal oxoalkoxides

Metal carboxylates

Metal amino alkoxides

Hydrolysis:

$$M\text{-}(OR)_n + H_2O \longrightarrow M\text{-}(OH)_n + R\text{-}OH$$

Condensation:

$$M\text{-}(OH)_n + M\text{-}(OH)_n \longrightarrow -O-M-O-M-O-$$

Figure 5. Illustration of Sol gel Proces

Table1. Comparison of bulk MIP and core shell MIP

Order	Properties	Bulk MIPs	Core shell MIPs
1	Synthesis process	Easier simple	More complex
2	Yield	Lower	Higher
3	Morphology	Irregular	Uniform sphere
4	Specific area	Smaller	Bigger
5	Distribution of binding sites	All over the bulk embedded deep non-uniform	Near to surface of cores and uniform
6	Adsorption capacity	Lower	Higher
7	Leakage of template	More	Lower
8	Elution process	Harder inadequate	Easier sufficient
9	Mass transfer process	Lower	Higher

Table 2. Application of carbon dots-based MIPs for the sensing of different analytes

Order	Synthesis method of CDs	Synthesis method of MIP	Template	References
1	One pot synthesis	Sol gel polymerisation	Dopamine	[105]
2	One pot synthesis	Sol gel polymerisation	Sterigmatocystin	[107]
3	Hydrothermal method	Sol gel polymerisation	Nifedipine	[110]
4	Hydrothermal method	Sol gel polymerisation	4-nitrophenol	[108]
5	Hydrothermal method	Sol gel polymerisation	Bisphenol A	[106]
6	Hydrothermal method	Sol gel polymerisation	Triclosan	[111]
7	Hydrothermal method	Sol gel polymerisation	Ketoprofen	[112]
8	Hydrothermal method	Sol gel polymerisation	Aspirin	[113]
9	Microwave method	Sol gel polymerisation	Tetracycline	[109]
10	Microwave method	Sol gel polymerisation	α-amanitin	[97]

11	Microwave method	Self-polymerisation	17β-oestradiol	[114]
12	Hydrothermal method	Self-polymerisation	Ibuprofen	[115]