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Molecularly Imprinted Polymer and its Application with Special Reference to Drug Delivery: An Analytical Study

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Abstract: *Molecular imprinting technology (MIT) is a method for creating synthetic receptors that bind to a target analyte with a high degree of selectivity and specificity. Chemists are under increasing pressure to design and fabricate synthetic receptors with high selectivity interaction with template molecules and denote self-assembly behaviour for the accumulation of bimolecular and biological species and structures due to the overwhelming need for molecular recognition in nature and complex matrices. Hence the researcher has undertaken this study to explore the polymerization process for molecular imprinting, to discuss the factors affecting Molecular imprinting, to find out the applications of molecular imprinting and to study the use of molecular imprinting in the drug delivery. The research shows that Molecular Imprinting Technology (MIT) may be utilized to create artificial receptors that have a high degree of selectivity and specificity for a certain analyte, making them suitable raw materials for a wide range of applications. Polymeric matrices generated by imprinting technique are Molecularly Imprinted Polymers (MIPs), which are powerful molecular recognition elements that may replicate natural recognition entities like antibodies and biological receptors.*

Introduction:

Polyakov first suggested the concept of molecular imprinting technology (MIT) in 1930. MIT is an experimental approach that includes creating synthetic receptor sorbents of a target molecule on a polymer network. The phrase "molecular imprinting technique" was coined by Alexander et al. “The construction of selective ligand in synthetic polymers where a template (atom, ion, molecule, complex or a macromolecular assembly including micro-organisms) is employed in order to facilitate recognition site formation during the covalent assembly of the bulk phase by a polymerization or polycondensation process with subsequent removal of some or all of the template being necessary for recognition to occur in the spaces vacated by the templating species”.

Molecular imprinting and molecular imprinted polymers (MIP) are appealing because they need few complex components, resources, or unit activities to perform. In order to create the cavities in the MIP, the polymer matrix was co-polymerized with functional monomers and cross-linkers while the target or template molecule was present. Structure predictability, global applicability, and precise target detection are just a few of the distinctive traits that set MIP apart. Numerous scientific and technological disciplines, including purification, chemobiosensing, separation science, drug administration, artificial antibodies, catalysis, enantiomeric identification, and degradation, have taken an interest in these molecules. Their superior adsorbency comes from features such as great physical stability, ease of preparation, cheap cost, and extraordinary toughness.

Molecular imprinting is a method for encoding molecular recognition templates onto polymer matrices with the use of template-shaped holes. The "lock and key" paradigm of substrate

recognition utilized by enzymes provides the inspiration for this method. An enzyme's active binding site has a certain geometric structure that makes it compatible with a given substrate. Enzymes are able to selectively bind to substrates whose shapes are a good match for their active sites, whereas substrates with shapes that aren't a good match are ignored. Similarly, molecularly imprinted materials are made by assembling functional monomers around a template molecule and then cross linking the resulting polymer network. An imprinted matrix (also known as a molecular imprinted polymer, or MIP) is formed when functional monomers self-assemble around a template molecule by interaction between functional groups on the template and monomers.

Objectives: The present study aims at the following-

- ✓ To study the polymerization for molecular imprinting.
- ✓ To discuss the factors affecting Molecular imprinting.
- ✓ To find out the applications of molecular imprinting.
- ✓ To study the use of molecular imprinting in the drug delivery.

Significance of the Study:

In molecular imprinting, the target molecule (or a derivative thereof) serves as a template around which a cast-like shell is formed by arranging and copolymerizing interacting and cross-linking monomers. At first, the monomers interact with the template in either a covalent or noncovalent complex. Binding sites complementary to the template in terms of size, shape, and location of the functional groups are exposed after polymerization and removal of the template, and are retained by the cross-linked structure. The polymer effectively acquires the ability to selectively rebind the template thanks to the imprinting of a molecular memory. Therefore, molecularly imprinted polymers (MIPs) have the capacity to recognise and bind particular target molecules, the defining characteristic of biological receptors. In this regard the present study is significant enough since it will be very helpful for the chemists, researchers and all others concerned to this.

MOLECULAR IMPRINTING POLYMERS BY POLYMRISATION:

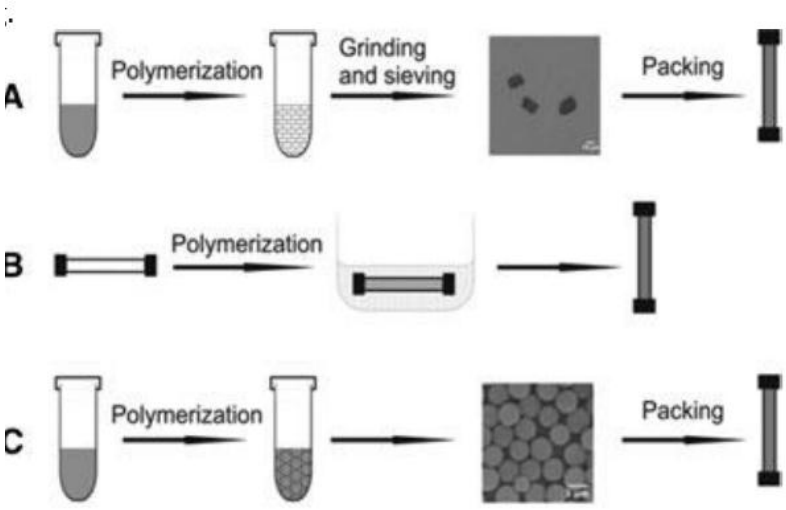
Precipitation polymeristion: Unlike conventional polymerization, precipitation polymerization takes place in a much greater volume of solution. Covalent molecular imprinting has been found to be more effective than non-covalent imprinting. Non-covalent imprinting, on the other hand, has the benefit of rapid guest binding and release. This led us to use a non-covalent strategy for the synthesis of the current set of imprinted polymers. In precipitation polymerization, MIP aggregates or microspheres with a diameter of a few tenths of a micrometre were produced. In precipitation polymerization, it was shown to be crucial to have the solubility parameter of the final polymer correspond with that of the porogen (solvent).

In-situ polymeristion: As the polymerization occurs directly in the chromatographic column, in situ polymerization is a straightforward approach to the preparation of MIPs (Hosoya et al., 1996 ; Zhang et al., 2003 ; Lin et al., 2006). Preparation of molecularly imprinted monoliths was pioneered by Matsui and colleagues (Matsui et al., 1993 ; Matsui et al., 1995) using the in-situ polymerization method. For creating chromatography and SPE stationary phases, its high porosity and permeability are advantageous. (Liu et al., 2005)

Bulk polymerisation: Depending on their intended use, molecularly imprinted polymers may be made in a number of different shapes and sizes. Solution polymerization, followed by mechanical grinding of the resultant bulk polymer to provide tiny particles, and sieving the particles into the necessary size ranges, with diameters commonly in the micrometre range, is the standard procedure for making MIP. This is the most common approach, and it has numerous benefits, particularly for beginners. In practise, it is quick and easy to implement, and it does not need specialised operator abilities or high-tech equipment.

Despite its convenience and the ease with which imprinting conditions may be optimised, the bulk polymerization approach has a number of limitations. When it comes to chromatographic

performance and MIP loading capacity, the uneven sizing and shapes of the particles formed after the final sieving stage have a detrimental effect since some interaction sites are removed during grinding. The grinding and sieving process is both time-consuming and wasteful, with estimates placing the proportion of usable polymer lost during this step at between 50 and 75 percent of the original bulk material. The high consumption of template molecules was a drawback of this technique since some of the polymer can only be utilized as packing material.



FACTORS AFFECTING THE MOLECULAR IMPRINTING:

Template: The imprinting strategy used is heavily dependent on the form, size, and chemical functionality of the template species. A wide variety of molecular shapes and functions have been imprinted from hundreds of different template species. In order to be compatible with free radical polymerization, a template should be soluble in organic solvents, contain electrostatic functions, and be chemically inert under polymerization conditions. Imprinting might be challenging to accomplish for bigger molecules. The imprinting process relies heavily on characteristics of the template species, yet these characteristics also tend to be the least flexible. When the template is removed, a void is created that is chemically and physically similar to the template species.

Functional monomer: For the imprinting process to work, it is crucial that the functional monomer have certain chemical properties. In order to facilitate the creation of robust non-covalent contacts between the functional monomer and the template, the monomer is chosen with care. Karim et al. have provided a comprehensive analysis of the methods used to far for optimising MIP design. We looked at the various methods utilised to reach the pre- and post-polymerization media and the interactions that take place there. In order to maintain stable monomer-template complexes throughout the imprinting process, the selection of functional monomers is crucial. The functional group is selected so as to enhance the template molecule's chemical activity. Templates containing acid groups are best served by monomers with little functionality. As an example, MAA is often utilised as a starting point for design.Vinylpyridine is the monomer of choice for templates with carboxylic acid moieties.

Cross-linking monomers: Making an impression requires a series of steps, the first of which is designing a recognition site and selecting an effective imprinting approach. The next phase is getting the polymer ready. The majority of imprinted polymers are created using free radical vinyl polymerization. The major characteristics of these polymers are their strong cross-linking, which is generally between 70 and 95 percent. This dense network of cross-links serves an essential purpose by providing the recognition sites with structural stability.

Solvent/ Process: The imprinting procedure and the MIP's physical condition (morphology, pore size distribution, pore structure, swellability, and toughness), as described by Sellergen and Shea, are affected by the quantity and kind of porogenic solvent employed during polymerization. The polymerization solvent plays many important roles: a) It stabilises template monomer pre-

polymerization complexes and so makes the pre-polymerization mixture more amenable to polymerization. d) It plays the role of a 'porogen', which regulates the polymer's porosity.

The capacity of the porogen to stabilize template monomer complexes is the primary mechanism by which it affects non-covalent imprinting. The intensity of contacts is expected to be affected by the hydrogen bond capacity and polarity of the solvent (porogen) utilized in the imprinting process. A lack of correlation between selectivity and polymer morphology was shown in a research by Sellergren and Shea, however a correlation between the hydrogen bonding capacity of porogen and polymer selectivity was found.

Initiator: The production of free radicals is the most typical starting point for MIP synthesis. In most cases, heat or light have been used to create free radicals. There are three stages to the polymerization mechanism: initiation, propagation, and termination. The formation of a heterodimer with free radical functionality by initiation, wherein a free radical produced by the breakdown of the initiator (AIBN) attacks the double bond of the vinyl monomer molecule; During polymerization, the reaction proceeds by transferring a chain between the free radical and a new monomer unit, and the chain quickly spreads by the addition of more monomers as the radical chain grows. The radical of two developing polymer chains may pair, removing the radical from the polymerization process and bringing about termination. This is only one of several possible mechanisms. One of two methods, combination or disproportonation, may bring about this result.

Temperature: Formation of monomer-template complexes relies on equilibrium, making them particularly sensitive to temperature. Several researches have looked at how polymerization temperature affects MIP efficiency. In comparison to polymer produced at higher temperatures, MIPs polymerized from polymers with better selectivity have a lower polymerization temperature. Photochemical polymerization is required for polymerization at lower temperatures.

Advantages of molecular imprinted polymers:

Molecular imprinted polymers (MIPs) have the capacity to recognize and bind to particular target molecules, two of the most crucial properties of biological receptors. Advantages of molecularly imprinted polymers over their biological analogues include, among others,

a) high physical resistance against external degrading factors, such as mechanical stress, high temperature and pressure, resistance against treatment with acids, bases, or metal ions, and stability in a wide range of solvents; b) antibody-like molecular selectivity.

b) They retain their molecular memory even after being repeatedly regenerated and utilised in the dry condition at room temperature for years.

It is possible to imprint polymers with chemicals for which it is difficult to produce natural antibodies. Therefore, molecular imprinting-prepared artificial receptors might be an appealing alternative to or supplement to natural antibodies and receptors.

Disadvantages of molecular imprinted polymers: There are a number of problems with MIPs. Sculpting the binding site in three-dimensional polymer networks may be challenging with conventional polymer monoliths because of their high density. The insufficient recognition qualities are the outcome of the poor mass transfer and persistent entrapment. The main disadvantages of these synthetic polymers are the variability in binding affinities, the sluggish mass movement in and out of the polymer matrix, the overall low binding affinity, the absence of a read out for complexation, and the trapped template slowly leaching out [18].

Applications of Imprinted Polymer

Solid-phase extraction, chromatographic separation, membrane separations, sensors, drug releases, catalysts, etc. all make use of molecularly imprinted polymers (MIPs) as materials of molecular recognition. MIPs are most often put to use as solid-phase adsorbents in high-performance liquid chromatography (HPLC).

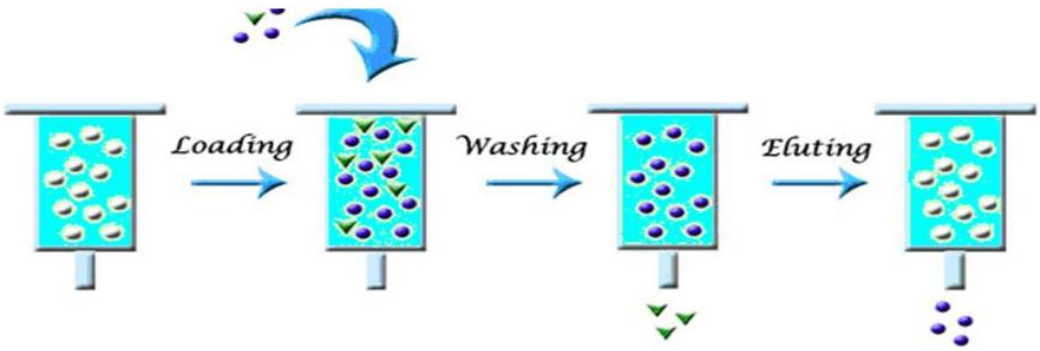
Separation: As new markets open up in sectors including the chemical and pharmaceutical industries, water purification, and waste-material treatment, the area of separations continues to grow. Affinity separation, solid phase extraction (SPE), and separation under severe circumstances (such as organic and toxic environments, low and high pHs, and high temperatures and pressures) are predicted to account for 1-3% of this market for MIP materials.MIP adsorbents have several applications, including protein purification, drug solid-phase extraction, taste ingredient recovery, and DNA/RNA/peptide/hormone/carbohydrate purification. MIPs are also useful for the separation of chiral chemicals, which have a role in fields such as fundamental research, drug design, optics, and polymer chemistry. The chemical industry finds MIPs appealing because to their potential to replace multistep enrichment and purification operations with a single-step separation on a MIP, even under harsh conditions such as those found in organic solvents.

Chronography, bibliographical references The most common applications of MIPs in separation are electro chromatography and solid phase extraction.

Sensors: When an analyte binds to a recognition element in a chemical sensor or biosensor, a chemical or physical signal is formed, and the transducer converts this signal into a measurable output signal24. Low stability, high cost, and a lack of enzymes or receptors that can recognise specific target analytic are some of the most common issues that have yet to be resolved in regards to biological materials used in biosensors. Since MIPs are more stable than biological receptors, they are a viable option for use in sensors. When a receptor or enzyme is not commercially accessible or affordable, MIPs may be synthesized to serve as a suitable alternative. Polymerization is also entirely compatible with micro fabrication, which is essential for sensor technologies. Herbicides, sugars, nucleic acid and amino acid derivatives, medicines, poisons, solvents, and vapours are only some of the substances for which MIP sensors have been designed.

SOLID-PHASE EXTRACTION:

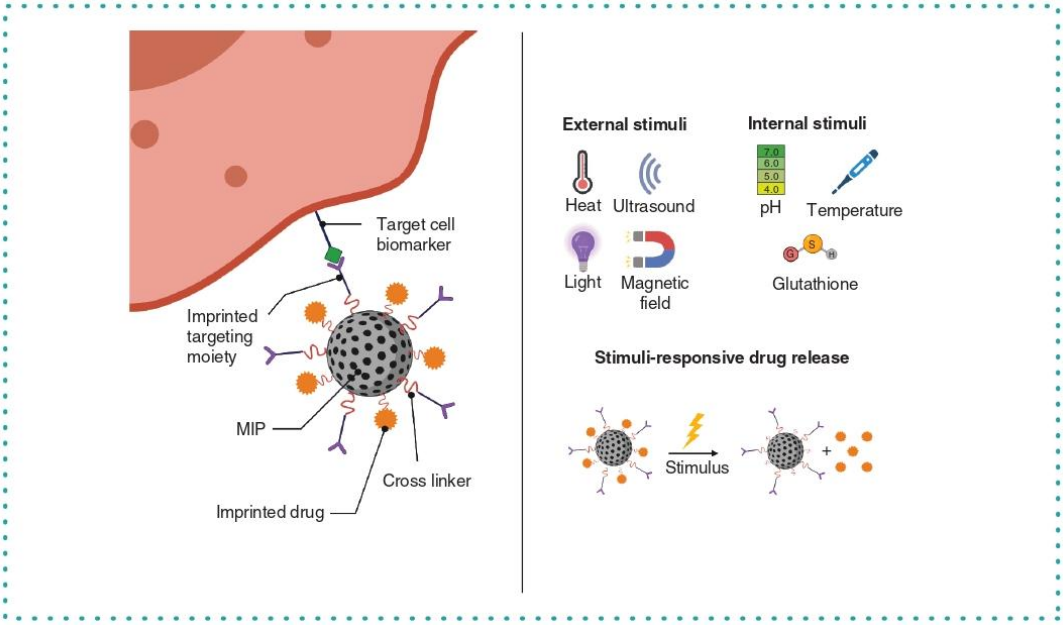
Another significant use of MIPs in analytical chemistry is in solid phase extraction (SPE). In both on-line and off-line processes, MIP for Solid-phase extraction (MISPE) has been used. For on-line operation, MIPs particles may be placed in an HPLC pre-column, while for off-line operation, they can be sandwiched between two frits in a cartridge. Directly integrated with particular analytical systems like HPLC, the on-line MISPE technique reduces the amount of sample handling, the amount of lost analytes, and the likelihood of contamination. In addition, the time required to prepare the samples for analysis is cut down drastically by using this procedure. Similar to traditional SPE, MISPE entails four basic steps: sorbent conditioning, sample loading, interference removal, and target analyte elution. The sample is loaded into the MIP and percolates through the sorbents. In order to maximize the amount of interactions between analytes and particular binding sites in the MIP sorbents, this solvent should have a polarity that is consistent with that utilized during polymerization.



MIPs & drug delivery:

DDS must control both the dose and the pace at which a medicine is administered. The medicine should ideally be carried to the proper spot within the body prior to release in order to minimize damage to healthy tissues and maximize absorption. There has been some research on using MIPs in

biological settings as drug delivery agents. They are well-suited for use in drug administration because of their excellent chemical and physical stability, simple and inexpensive manufacture, and extended shelf life. MIPs' versatility as DDS stems from their amenability to fictionalizations, which allows them to bind selectively and with high affinity to almost any kind of drug molecule. MIPs are stable in harsh environments and may prevent enzymes from degrading a medication before it reaches its target. To determine whether or not MIPs might transport insulin to GI cells, Paul et al. synthesized MIPs imprinted with insulin as a template molecule. Indeed, these MIPs showed promise as oral DDS for diabetic rats after being delivered in vivo. The MIPs prevented the medication from degrading, improved its absorption by GI epithelial cells, and prolonged its half-life.



One of the greatest benefits of MIPs is their capacity to increase a drug's half-life and regulate its pharmacological action in the body. A medicine's continuous release may lessen the number of times it has to be administered and any unwelcome effects that may result from having a high concentration of the drug in the body. Since nearly any form of template may be utilized, the no covalent strategy for interactions between the drug and the functional monomers is the most often employed way for MIP synthesis in DDS. Altering the strength and kind of contacts between the template and the functional monomers may maintain drug release, but the binding and release characteristics of the MIPs are also impacted by the cross-linker of choice.

Oral, inject able, ocular, and transversal MIPs are currently under development in the field of DDS. As an alternative to the several daily applications of eye drops, molecularly imprinted hydro gels or therapeutic contact lenses have been shown to be effective in providing prolonged medication administration to the eye. In rabbits, antihistamine ketotifen imprinted on contact lenses showed much greater bioavailability and residence duration than drug-soaked lenses or eye drop therapy. MIPs imprinted with vancomycin were able to release the medication at a significantly slower pace and over a much longer time period compared to nonimprinted particles, making them ideal for use in coating implants for sustained drug administration to prevent bacterial infections. A liquid crystalline monomer was added into the MIP structure to provide a floating characteristic for prolonged drug administration in the GI tract. This increased the drug's bioavailability in mice and rats in vivo by increasing its residence duration in the stomach.

Conclusion:

From a materials standpoint and an application standpoint, molecular imprinting has expanded substantially during the last decade. There is, however, a great deal of space for additional development. The binding site homogeneity and water compatibility of MIPs, as well as the feasibility of synthesizing MIPs specific for proteins, are now regarded major difficulties, and are

being addressed by research organizations all over the globe. Other crucial aspects include the manufacture of extremely tiny and quasi-soluble MIPs, near in size to proteins, and the ideation of composite materials based on MIPs to include other fascinating features into the material.

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