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APPLICATION OF MOLECULAR IMPRINTED POLYMER IN EXTRACTION AND SEPARATION OF PLANT BASED ACTIVE COMPOUNDS

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Abstract:

Molecular imprinting technique is becoming an appealing and prominent strategy to synthesize materials for target recognition and rapid separation. It has been used in recent years to separate active chemicals from diverse plants and has produced pleasing results. This review aims to provide a concise overview of molecular imprinting polymers and their significant use in the extraction and separation of various plant based active compounds, such as flavonoids, alkaloids, fragrance ,anti-inflammatory, vitamins ,phenylpropanoids, anthraquinones, , terpenes, steroids, diketonesand chemicals. These findings will serve as important tool to stimulate further research into this intriguing and practical domain. Molecular imprinting approach is very attractive, popular and appealing method of generating materials for target recognition and precise separation. Recently, It has been used to separate variety of active molecules from various medicinal plants.

Keyword: *molecular imprinting technology, MIP, molecular imprinted polymers, extraction, separation*

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INTRODUCTION:

For biological applications, molecularly imprinted polymers (MIPs) are now utilized and developed extensively. Molecularly imprinted polymers (MIPs) are currently widely used and further developed for biological applications. The MIP synthesis procedure is a key process, and a wide variety of protocols exist. The templates that are used for imprinting vary from the smallest glycosylated glycan structures or even amino acids to whole proteins or bacteria. The low cost, quick preparation, stability and reproducibility have been highlighted as advantages of MIPs **[1].**

MIP can be defined as the process of making of a molecular lock that fit-in a molecular key. It can be understand as a tailored binding site which perfectly fits the template molecule**(2).**

Molecular imprinting technique (MIT) is considered as a promising technique because it can recognize both biological and chemical molecules including proteins ,pollutants **[3],** and food chemical residues **(2).** MIT is becoming more and more significant and popular and has gained enormous attention due to its prominent advantages such as its spectrum of high selectivity, stability, wide practicability, cost and durability**(5).** Nowadays, it's widely used in various fields, such as pharmaceutical industry**[3],** food chemicals detection **[3],** and extraction of plant components **[4].**

MIT, includes three basic steps. Firstly, template molecules (atoms, ions, molecules or polymers) bind to the functional monomers through prearrangement or self-assembly to form template monomer complex. Then the template monomer complex is allowed to polymerize in the presence of the cross-linking agent to generate a three-dimensional polymer network. After polymerization, the template molecule in the polymer is removed by chemical reaction leaving specific recognition sites complementary to the template molecule in respect of shape, size and functional groups**(4).**

MIT can be categorised as covalent MI, non-covalent MI, and semi-covalent MI based on various types of interactions between template molecules and functional monomers [5]. The synthetic methods of MIPs include bulk, epitope, and surface imprinting, which are further divided into soft lithography, template immobilisation, surface grafting imprinting, and emulsion polymerization depending on the polymerization process. Reversible covalent contacts are used in covalent MI to connect template molecules to useful monomers. Following polymerization, the covalent bonds are broken to release the template molecules and create the distinct recognition cavities. The same covalent connections are created when the guest molecules rebind. The method's utilisation of templates is constrained since covalent interactions must be quick and reversible**. [5].**

The commonly used methods for synthesizing MIPs include bulk polymerization, precipitation polymerization, suspension polymerization, emulsion polymerization, surface MIT which can again further divided into five kinds: emulsion polymerization, sol-gel polymerization, chemical grafting method, sacrificial carrier method and active controlled radical polymerization

Bulk polymerization, the most commonly used method, refers to adding templates, functional monomers, crosslinking-agents and initiators into solvents to synthesize polymers. The apparent advantages are simple operation, high purity and easily controlled reaction [17]. MIPs synthesized with bulk precipitation generally exhibit dissatisfactory binding site accessibility. MIPs made with this method shows irregular shape and limited adsorption.

Precipitation polymerization is a process that produces MIPs that can be precipitated on their own and do not dissolve in the reaction liquid. This technique is one of the simplest ways to make micro- and nanosphere particles of uniform size, providing better uniformity and more surface area. Furthermore, monomers can self-polymerize as a result of precipitation without the need for a stabiliser. Unfortunately, for precipitation polymerization to work properly, a lot of organic solvents must be used, and there must be tight guidelines. The creation of molecularly imprinted adsorbent materials in an aqueous phase is possible using suspension polymerization [17]. The MIPs made using this approach have very large specific surface areas, which facilitate molecule binding and shedding. The downside is that the recognition of suspension preparation is poor.

When an emulsion is created through mechanical stirring combined with emulsifying agents, functional monomers, template molecules, and other materials are then added to the oil-water phase to complete the polymerization process. Initiators are additionally used to kick off the polymerization. This approach produces MIPs with pleasing characteristics such as consistent particle sizes, regular forms, and good dispersion **[7].**Yet, the insufficient removal caused by the use of emulsifying agents may result in lower product purity.This present study shows that application of MIP technology has great potential in separating and extracting the plant based active compounds.

Purification of Vanillin by MIP

Ibrahim et al **(2009)** perfomed Purification of vanillin by a molecular imprinting polymer technique. In Separation and Purification Technology of vanillin from soda lignin, extracted from the black liquor of oil palm empty fruit bunches (EFBs) with 20% (v/v) sulfuric acid may be negated by the high impurity content in the vanillin obtained. A molecular imprinting polymers (MIPs) technique was developed for vanillin to remove the impurities attached to it. A synthesis method was used in preparing the MIPs, where impure vanillin molecules were used as the template, dimethylsulfoxide (DMSO) as the solvent, and methacrylic acid (MAA) and ethylene glycol dimethacrylate acid (EGDMA)working as the monomer and cross-linker. The results were confirmed by gas chromatography (GC), mass spectrometry (MS), Fourier transform infrared (FTIR) spectroscopy and thermal gravimetric analysis (TGA) of the sample against a standard vanillin**(7).**Present study provide evidence that MIP was undoubtedly a great method.

Separation and Detection of Curcumin by MIP

Ranjbari et al **(2023)** performed a study on Molecularly-imprinted polymers for the separation and detection of curcumin Here in the Curcumin, a polyphenol obtained from *Curcuma longa*, has been widely used in medical science because of its high healing and non-toxic pharmacological properties. Further, different methods have been proposed for the analysis (detection) of curcumin in a variety of sample. Unfortunately, these method showed poor selectivity for curcumin. However, molecularly-imprinted polymers are currently gaining considerable attention, because of their ability to enhance both the selectivity and sensitivity when used to identify curcumin. The integration of MIP using various techniques (*e.g.*, sensors) has led to the creation of a powerful method for the analysis of chemical compounds. In this study they have provided a summary of curcumin's physicochemical and pharmacological properties, along with recent detection techniques. Finally, this present study provides vital support on molecularly-imprinted polymers used for the detection as well as separation of curcumin.out of various technique(eg magnetic and nanoparticles) they showed that the MIT was appeared to be a very versatile and attractive method for the separation (isolation) and detection of curcumin**(3).**

Synthesis and evaluation of Ginsenosides using metatemplate MIP

Xue at al **(2023)** Recently performed his work on the Synthesis and evaluation of ginsenosides imprinted polymer based chromatographic stationary phase using multitemplate in MIP**(39).** As we all are familiar with the fact that recently MIT has gained great interest in preparing novel stationary phases, and the resulting materials named molecularly imprinted polymers coated silica packing materials exhibit good performance in separating variety of analytes based on their good characteristics (including high selectivity, simple synthesis, and good chemical stability). Till now, stationary phases based on molecularly imprinted polymers have typically been created using mono-template. The problems of low column efficiency and constrained analytes are always present in the final products, and the cost of ginsenosides with high purity was very high. In this study, the multi-templates (total saponins of folium ginseng) technique was employed to construct ginsenosides imprinted polymer-based stationary phase in order to address the disadvantage of molecularly imprinted polymers-based stationary phases discussed above. The resulting stationary phase of silica with ginsenosides imprinted on the polymer has a better spherical shape and appropriate pore architectures. Also, folium ginseng's total saponins cost less than other ginsenoside varieties. Moreover, the ginsenosides imprinted polymer-coated silica stationary phase-packed column performed well in the separation of ginsenosides, nucleosides, and sulfonamides**(5).**

Separation of Acteoside usingA-MINMs

Acteoside (ACT) and echinoside (ECH) had similar structure and property in the phenylethanoid glycosides (PhGs), thus the selective separation of ACT and ECH was a bottleneck problem. In this study, ACT was used as template molecule, and multilayer-functionalized of molecularly imprinted nanocomposite membranes (A-MINMs) were designed to efficient ACT separation. The A-MINMs were fabricated by using polydopamine (PDA), polyethylenimine functionalized mesoporous silica (PEI/MCM-41) and ACT imprinted layer to modify the surface of polyvinylidene fluoride (PVDF). The PDA layer was a stable surface adhesive, and the filler PEI/MCM-41 was uniformly bonded to the PVDF membrane surface, thus constructing the second layer on the membrane surface. The PEI/MCM-41 layer adjusted the pore uniformity of the membrane surface, and contained abundant amino groups, which provided an ACT imprinted platform to trigger the imprinted polymerization to form an imprinted layer. The ACT imprinted layer had a large number of ACT imprinted sites and cavities, which could specifically recognize ACT, realizing the efficient ACT separation. The results indicated the high rebinding capacity (108.74 mg/g) and permselectivity ($\beta_{ACT/ECH} = 9.43$) of A-MINMs. Therefore, multilayer-functionalized A-MINMs has a potential application prospect in the field of natural product separation membrane materials**(10).**

Adsorption of chrysin using a magnetic surface MIP

As an vital naturaly occuring nutrient-like substance, chrysin is highly desirable in the field of health food. Here, to achieve the specific and efficient adsorption of chrysin, a magnetic surface molecularly imprinted polymer (chrysin/SMIPs) was fabricated by free radical polymerization of methacrylic acid onto the surface of functionalized magnetic Fe_3O_4 nanoparticles. The obtained chrysin/SMIPs showed favorable binding ability towards chrysin with 35.27 mg·g^{-1} maximum adsorption capacity in 20 min, prominent reusability with 9 cycles of adsorption–desorption and superior specific recognition with imprinting factor (*IF*) of 2.87 and selectivity coefficient (*K*) of 8.74, 5.64 and 8.64 corresponding to the interferents of genistein, daidzein and quercetin, respectively. Moreover, the chrysin/SMIPs showed high recoveries (91.13 % to 95.12 %) and precisions (RSDs from 2.51 % to 1.32 %) in the extraction of chrysin from real propolis samples.Hence, chrysin/SMIPs is highly promising for the selective enriched adsorption of active compounds.

Application of molecular imprinting technology using Cyclodextrin monomer

By joining starch molecules in a cyclic ring, cyclodextrins (CDs) are created. It is made up of five (1, 4) or more joined D-glucopyranoside units. CDs feature truncated cone shapes that are toroidal, hollow, and have hydrophilic edges on the outside and hydrophobic cavities inside. In cyclodextrins, there are a number of hydroxyl groups that can act as active sites for a variety of interactions. They are capable of being cross-linked or derived to produce monomers that can form linear or branching networks. They can also create inclusion complexes with both organic and inorganic guest molecules, which can alter their physicochemical characteristics. Modifying the imprinting process may result in molecularly imprinted polymers that are reliable, durable, cost-efficient, stable, and selective. Hence, molecularly imprinted polymers are gaining popularity**(9).**

Application of MIP in Separation and purification of flavanoids

In the realm of developing and researching natural products, there has been an increase in interest in the isolation and detection of flavonoids from various natural products. Molecularly imprinted polymers (MIPs) are suggested as effective adsorbents for the selective extraction and isolation of flavonoids from complicated materials because of their great specificity. The use of MIP-based sensors for the detection of flavonoids as well as the separation and purification of flavonoids using molecular imprinting have not yet been the subject of a thorough review study. Here, we evaluated the standard techniques used to create MIPs for flavonoids, including emulsion polymerization, surface imprinting, precipitation polymerization, and bulk polymerization.This review aim to provide helpful suggestions for the advance preparation methods of MIPs for the extraction of flavonoids and future applications of MIPs for the detection of flavonoids from natural products and biological samples**(11)(18).**

Applicatin of MIP in green chemistry

A potent approach for synthesis of tailored receptors inside polymeric matrices is molecular imprinting. First , Polyakov reported on it for the first time in 1934, it is still a highly difficult research field today. In a number of applications, including immunoassays, affinity separation, sensors, and catalysis, where selective binding is necessary, molecularly imprinted polymers (MIPs) have been employed successfully. In addition to stricter regulations on the use and release of chemicals into the environment and the presence of impurities on final materials, conventional methods used in MIP production continue to use significant amounts of organic solvents, which will, in our opinion, encourage the use of new cleaner synthetic strategies, particularly with the application of the principles of green chemistry and engineering. Ionic, supercritical carbon dioxide, and microwave This study suggested and encouraged the use of MIP in extraction ,synthesis and purification of active compounds sustainable development in future**(12).**

Application of MIP as a tool in medicinal plant analysis

Characterization and extraction of plant secondary metabolites are crucial in the field of agriculture, food pharmaceutical industry. In this regard, the current applied analytical methods are too expensive and time-consuming, hence, choosing a suitable approach is essential for optimum results and economic suitability. One of the most recently considered method used to characterize new types of materials is MIPs. Out of the several applications of MIPs the main is the identification and separation of various plant-derived compounds, such as secondary metabolites, and pesticides chemical residues. The present review describes and suggests the application of MIPs as a tool in medicinal active plant material analysis and focus on plant secondary metabolism**(13).**

Selective adsorption of sinnapic acid using MIP

In order to preferentially extract sinapic acid from squeezed rape seed extract, a new and simple hydroxyapatite coating imprinted with sinapic acid was made using deep eutectic solvents (DESs). In the creation of MIPs, various DESs served as functional monomers and cross-linkers. The core was chosen to be hydroxyapatite, and the imprinting layer was uniformly coated on top of it. Batch adsorption studies revealed that the MIPs had an adsorption capacity of 121 mg g-1 and had exceptional recognition ability. The created imprinted materials could be recycled and utilised again and again without suffering a major loss in adsorption capacity. The proposed approach was subsequently used for the selective extraction of sinapic acid in squeezed rape seed extract due to the aforementioned good results in comparison with previous existing methods**(14).**

Detection of geraniol using (MIP) based quartz crystal microbalance (QCM) sensor

As we all know that Geraniol is a commercially available ,a significant terpene alcohol found in the essential oils of a variety of aromatic plants. This molecule is known for its the flavor and fragrance in the industries, and a common ingredient in consumer cosmetics products. At present to detect geraniol in real samples, silicone sealant, a readily available commercial product, was used as the polymer to prepare a molecularly imprinted polymer (MIP) based quartz crystal microbalance (QCM) sensor and is presented in this paper. Optimum ratio of sealant was dissolved in dichloromethane and then geraniol was added as the template molecule to synthesize the coating material of the sensor. The developed sensor showed significantly good sensitivity and selectivity to geraniol and was employed to detect the concentration of geraniol at ppm level in different palmarosa essential oil samples. Good correlation was obtained with the responses from gas chromatography.Hence The Present study suggest the future prospects of MIP in detection of variety of flavored active compounds**(16).**

Extraction of Anthraquinone from rhubarb using MIP

A simple method based on matrix solid-phase dispersion for selective extraction of anthraquinones from rhubarb,few samples was developed using a molecularly imprinted polymer as sorbent. The MIPwas preparedby using emodin as the template molecule, methacrylic acid as the functional monomer, and ethylene glycol dimethacrylate as the cross-linking agent**(35).** The prepared polymer was characterized by SEM and FTIR spectrometry. Further Isothermal adsorption and dynamic adsorption experiments were performed too .The best extraction conditions for anthraquinones were obtained at a ratio of molecularly imprinted polymer to sample of 1:1, a dispersion time of 5 minutes, with 5% aqueous methanol as the washing solvent, and an elution solvent of methanol-acetic acid (99:1, v/v). Once the matrix solid-phase dispersion process was optimized, the extract was reacted with 8% hydrochloric acid for hydrolysis. The anthraquinones extracted from rhubarb were determined by liquid chromatography**(36).** The detection limits of chrysophanol, emodin, physcion, and aloe-emodin were 0.23, 0.24, 0.28, and 0.27 μg mL−1, respectively. The proposed method was compared with the method in mentioned in Chinese pharmacopoeia, and the results show that the extraction yield of anthraquinones obtained by molecularly imprinted polymer–matrix solid-phase dispersion method was higher than that.Furthermore, the proposed method is quicker and easier and can achieve extraction and purification within the same system**(25).**

Extraction of Galegine using column chromatography with MIP

Southeast European native alega officinalis L. (Papilionaceae) is used to cure a number of illnesses, including diabetes. Galegine, a guanidine alkaloid, is one of many potent chemicals found in this plant's extract. This useful substance was obtained in this study using column chromatography and a molecularly imprinted polymer (MIP) approach. By employing silica gel as the stationary phase in a column chromatography, the extracted components were separated. Once the mobile phase was totally non-polar hexane solvent for the elution of components from the galegine extract, the solvent's polarity was increased until all of the remaining components were eliminated. 11 fractions were finally obtained. The separated components were identified using the thin-layer chromatography (TLC) technique. Next, the Galegine was extracted along with combining the column chromatography with MIP.therefore the present study shows that the isolation and purification of galegine was increases up to 17 time as that of MIP alone**(17).**

Extraction of curcumin using MIP

Due to its therapeutic and non-toxic pharmacological qualities, curcumin, a polyphenol derived from Curcuma longa, has been utilised extensively in medicine. Several approaches have recently been put up for the analysis (detection) of curcumin in numerous sample matrices. Sadly, there is little curcumin selectivity in these approaches. Nevertheless, molecularly imprinted polymers are currently attracting a lot of attention because of their ability to improve curcumin detection methods' sensitivity and selectivity. A potent methodology for the examination of chemical substances has been developed through the inclusion of molecularly-imprinted polymers utilising a variety of techniques (for example, sensors). We initially discuss molecularly imprinted polymers and their physicochemical characteristics in this paper. Here present study provides a quick review of curcumin's physicochemical, pharmacological, and most recent detection methods used in its extraction(33).

Selective enrichment of Rutin from Sophora japonica using MIP

Due to its great biological and commercial significance, rutin (RT), a widely distributed natural flavonoid compound, has frequently been used as an important active ingredient. A novel class of magnetic molecularly imprinted polymers (HB-TI-MMIPs) with numerous, highly-affine, and uniformly-distributed binding sites were purposefully developed for the selective enrichment of RT from Sophora japonica. These polymers were inspired by the structural characteristics of densely packed bayberry and well-oriented honeycomb. The imprinted nanoparticles' physicochemical characteristics, adsorption efficiency, and polymerization conditions were all thoroughly examined. The improved HB-TI-MMIPs exhibit good selectivity for RT, a high adsorption capacity, and a quick adsorption rate. While this was going on, the suggested analytical technique, which utilised HPLC and HB-TI-MMIPs as adsorbents, was effectively used to enrich and detect RT from Sophora japonica with high recoveries (87.2-94.6%) This study suggest the future potential of MIP in the extraction of several medicinally active plant compounds**(18)(23).**

Extraction of QUERCETIN an antioxidant from onion peel

The present study performs the valorization of the onion solid waste (i. e. peel) by extracting quercetin (Qu) compound, as a natural antioxidant food ingredient**(40).** It is used as a raw material in the pharmaceutical, cosmetic and chemical**(41).** Onion pee is a highly rich source of Quercetin that is a valuable source of many useful biological properties, including antioxidant, anti-inflammatory, antiviral, antibacterial and antimicrobial properties.Furthermore, Quercetin molecular-imprinted polymer nanoparticles (Qu–MIP NPs) and its corresponding non-imprinted polymer (NIP) were prepared using precipitation/polymerization method. The prepared Qu–MIP NPs and its corresponding NIP were characterized using Fourier transform infrared spectrometer, scanning electron microscopy and high-resolution transmission electron microscope. The prepared Qu–MIP NPs and its corresponding NIP could successfully rebind Qu at binding capacities of 60 and 10.0 mM/g, respectively. Thus, the prepared Qu–MIP NPs could successfully recover 260 mg Qu from 1 kg onion peel.The present resreach provide an approach in utilizing onion solid waste in order to recover a valuable compound**(19)(22).**

Extraction of Polydatin

Precipitation polymerization was used to create molecularly imprinted polymers (MIPs) based on polydatin. Discussion of functional monomers, porogens, and the molar ratio of template-functional monomer-cross linker helped to optimise the synthesis process of MIPs. The next step was to create MIPs using polydatin as the template, 4-vinyl pyridine as the functional monomer, ethylene glycol dimethyl acrylate as the cross linker, acetonitrile as the porogen, and a 1:10:20 molar ratio of template, monomer, and cross linker. The macroscale and chemical bond of MIPs were examined using scanning electron microscopy and a Fourier transform infrared spectrometer. Static, dynamic, and selective studies were conducted to examine the adsorption capacity and selectivity of MIPs to polydatin.hence this study shows that using MIP selective enrichment of polydatin can be done from biological and plant source(20).

Adsorption of tocopherol using MIP

Puoci, F. et al.(2008) synthesized MIPs using α-tocopherol as template, methacrylic acid as functional monomer, ethylene glycol dimethacrylate as crosslinker and AIBN as initiator. The sorption of αtocopherol, vitamin A and β-carotene was evaluated in acetonitrile and ethanol-water (6:4, v:v) and higher sorption efficiencies were obtained in ethanol-water (6:4, v:v) environment. Standard solutions were prepared such that the calibration interval for all analytes was 0.5 µg/mL -25 µg/mL. Limit of quantification (LOQ) of α-tocopherol, vitamin A and β-carotene are 68 ng/mL, 250 ng/mL and 447 ng/mL, respectively.This study showed the relevance of MIP in drug delivery enhancement(21)(22).

CONCLUSION AND PERSPECTIVE:

In recent years, MIT is gaining more and more attention and popularity for its fabulous and versatile properties in various fields like pharmaceutical ,agriculture, food and chemicals. This review introduced the recent application of MIPs in separation and extraction of variety of active compounds from plants, having high economic and commercial utilities such as flavonoids, organic acids, alkaloids, vitamins , phenylpropanoids, anthraquinones, phenolics, terpenes, steroids, and antinflammatory. The separating methods based on MIPs possessed extraordinary advantages compared with traditional methods and provide future prospects to the researcher to develop more economical , stable and reusable methods. Present study further suggest that MIP method is one of the most effective and efficient in extraction of several flavanoids, Terpenes, antioxidants, fragrance and flavor providing substances, anti-inflammatory vitamins and chemicals from different plant sources.

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