Radiation induced synthesis of molecularly imprinted polymers

Moleküler baskılı polimerlerin radyasyonla başlatılan sentezi

Review Article

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ABSTRACT

Tunable properties fascinate scientists because of the opportunity to develop functional materials for stimuli-responsive, sensing and biomimetic applications. Over half a century ago, advances allowed the realisation of molecularly imprinted polymers.They enable to specifically target sugars, pesticides, herbicides, viruses, drugs and amino acid together with their derivatives.In fact, due to their simplicity, ability of building robust polymer networks, reusability and low costs, molecularly imprinted polymers (MIPs) still are of great interest both in academia and industry.They enable the use of lot of techniques for their implementation although our attention will be addressed to the ones realised via gamma-irradiation.

Key Words
Molecularly imprinted polymers, gamma irradiation, surface imprinting.

ÖZET

Kontrol edilebilir özellikler uyarılara tepki veren, algılayıcı ve biyo-taklitçi uygulamalar için fonksiyonel malzemelerin geliştirilmesi imkânı açısından bilim adamlarını etkiler. Yarım yüzyılı aşkın bir süre öncesinde gelişmeler, moleküler baskılı polimerlerin anlaşılmasına izin vermiştir. Bunlar şekerleri, pestisitleri, herbisitleri, virüsleri, ilaçları ve amino asitlerlerle birlikte onların türevlerini özgül olarak hedef alabilirler. Her ne kadar kolay olmaları, sağlam polimer ağların hazırlanabilmesi, tekrar kullanılabilirlik ve düşük maliyetlerine bağlı ise de moleküler baskılı polimerler hem akademi hem de endüstride halen büyük ilgi alanıdırlar. Bizim ilgimiz gama ışınlaması kullanılan yöntemleri kavramaya yönlenmiş olmasına rağmen uygulamaları için pek çok tekniğin kullanımına olanak sağlarlar.

Anahtar Kelimeler
Moleküler baskılı polimerler, gama ışınlaması, yüzey baskılama.

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INTRODUCTION

Molecular recognition is of great importance in living-systems such as antibody/antigen recognition, enzymatic catalysis, and signal transduction. It also plays a fundamental role in nucleic acid interactions such as replication, transcription, and translation. These features are mainly based on weak and reversible non-covalent interactions, including hydrogen and ionic bonding, van der Waals forces, hydrophobic and hydrophilic properties.

One of the most promising approachesfor molecular recognition is molecular imprinting, mainly related to the polymerization of functional monomers in presence of a template molecule.

To understand the molecular imprinting technique, we need to go back to Pauling's studies on the formation of antibodies [1] in 1940s. The recent interest in molecular imprinting is however related to the separation of a racemic mixture through covalent bonds between the template molecule and the functional monomer [2]. In this study, the separation of racemic mixture was achieved through covalent imprinting approach in which interactions between template molecules and functional monomers are based on covalent bonds. Research in molecular imprinting accelerated with a study belongs to Mosbach et al. which reports a simpler method than covalent imprinting [3]. This approach, which is called as non-covalent imprinting, contains non-covalent interaction between template molecule and functional monomers.

Molecularly imprinted polymers with a wide range of applications such as solid-phase extraction, drug delivery, catalysis, chiral separations, capillary electrophoresis, selective sorption, various types of sensors, and membrane separations can be prepared in different physical forms by using various polymerizations and grafting methods. Bulk polymerization [4], molecularly imprinted particles [5] and membranes [6], grafting of MIPs onto any support materials including particles [7] or fibres [8] can be achieved.

The first approach was based on the synthesis of MIPs as a bulk material. After grinding, the small undefined shaped pieceswere used in continuous and batch systems as recognition materials [4, 9]. This technique is simple and fast although disadvantages like waste of useful material and destruction of some recognition/binding sites during grinding and sieving [10] needs to be taken into consideration.

On the other hand, molecularly imprinted particles with regular shape and narrow size distribution are synthesised by multi-step swelling, emulsion, suspension and precipitation polymerization [11]. Each method has advantages and disadvantages. Highly reproducible results can be obtained by using suspension polymerization which is suitable for large scale production. The main disadvantages of this method are the phase partitioning of complicates system and the necessity of special surfactant polymers. Particles obtained using multi-step swelling polymerization technique are comparatively monodisperse in size and shape and well suited for chromatographic applications, however, fairly complicated procedures and reaction conditions are required. Selectivity can be decreased by the aqueous suspensions used in this technique due to their interfering effect on to formation of stable pre-polymerization complexes. Precipitation polymerization is a simple methodology letting the realisation of high yields of particleswith a uniform size. In regard to precipitation polymerization, well defined properties in terms of size and porosity can be obtained by changing the polymerization conditions [10]. Their high active surface area provides improvements in the recognition and specific selectivity properties of MIPs [12].

Surface grafting of MIP layers onto any support materials has been very attractive especially in sensor applications [13], surface modification [14] and extraction technologies. Grafting of MIPs onto different surfaces increases the reachability of binding sites and provides occurrence of binding and specific selectivity in two dimensions [15]. This method avoids the waste of bulk materials and directly provides coatings on the surface of fibres [8] or transducers. At

the same time, the grafting approach gives the opportunity to alter material properties without any change in their bulk properties [10]. It is possible to use pre-synthesized beads [16], non-woven fabrics [8], macro-porous membranes [17] as support material.

When realising MIPs, the most commoninitiation methodsare thermal [18] (at different temperatures, from 0 to 60°C [20]) or photo creation [19] of free radicals. These methods let the synthesis of MIPs with good recognition properties, albeit their selectivity mostly depends on the polymerization temperature. In fact, the lowest it is, the highestseparation factors are obtained [20,21] due to the stabilization of pre-polymerization complexes between template molecule and functional monomers.

Beyond these approaches, high energy radiation, such as gamma rays, electron beams and X-ray, can form very reactive intermediates in free radicals or ions form, readily enablingtheir use in reactions. For example, polymerization via gamma rays allows controlling reactions while supplying catalyst free initiation. It can also be used to alter the surface properties by grafting or cross-linking polymers.

In this review, our attention will be focussed on the comparison between thermal and photochemical initiation methodsover gamma irradiation,able to provide free-initiator techniques through the continuousformation of radicals byradiation.

Synthesis of MIPs in bulk

Thermal and photochemical techniques lead to obtain imprinted polymers with satisfied qualities, even though their selectivity strongly depends on the polymerization temperature. Because the arrangement of the functional monomers around the template molecule can be affected by polymerization temperature. Due to the thermal destabilization of the complexes between the template molecule and the functional monomers, separation factors are higher as the polymerization temperature is lower [18].

The initial studies on radiation induced molecularly imprinted polymers started in 1997. Milojkovic and co-workers fabricated MIPs via gamma irradiation initiation by using (+)-menthol as a template molecule. Menthol was chosen due to the weak association to methacrylic acid (MAA). The adsorption isotherms of menthol and camphor (test molecule) from n-hexane on MIPs and control polymers (non-imprinted)showed the selectivity of MIPs. This study washowever showing that the optimization of an imprinting system via radiation polymerization needs to be explored more in terms of dose and absorbed dose, as well as temperature.

It is also worth mentioning the works reported by Sreenivasan et al, Uezu et al on the use of gamma irradiation in order to improve the efficiency of MIPs [23-25] due to the absence ofextra additives or initiators. For example, 2-hydroxyethyl methacrylate (HEMA) based MIPs were investigated to detect salicylic acid in urine [24,25] using phthalic acid as a control molecule. It is indicated that salicylic acid was absorbed up to 20 μg by MIPs while the non-imprinted polymer was absorbing up to 3.7 μg, both in human urine. When phthalic acid was used, the MIPs showed similar absorption behaviour as the non-imprinted ones, due to trapped phtalic acid in the polymer matrix. Furthermore, HEMA-based polymers were investigated to address the interaction with cholesterol via gamma radiation induced molecular imprinting as well [24]. The recognition efficiency of MIPs was demonstrated in solutions of cholesterol, testosterone and their mixtures. The absorption of cholesterol per 100 mg of MIP was reported as 392±6 μg. Testosterone, which wasused as a test molecule, has nearly the identical size of the template molecule in terms of resolving the adsorption behaviour of pores, yet they do not really influence the uptake of molecules. Moreover, Sreenivasan and Sivakumar reported the evaluation of HEMA based MIPs prepared by gamma irradiation in the presence of two different template compounds: salicylic acid and hydrocortisone in poly(2-hydroxy ethyl methacrylate) [26]. The results showed that the monomers could pre-arrange more effectively around salicylic acid compared to hydrocortisone which is relatively bulkier. In this work the possibility of creating recognition sites more

than one compound was discussed and reported that such systems can be used in the design of sensors having the ability to sense more than one compound at same time.

Güven et al have studied glucose MIPs using different types of cross-linkers and varying the amounts of template molecule, while exploring the irradiation dose effect, in an attempt to elucidate the effectiveness of imprinting technique [27]. Cavity size of MIPs was inspected by positron annihilation lifetime (PAL) measurements in which a sandwich arrangement (sample-source-sample) was used. They found that the mean free-volume hole radius, R, change in case of high concentrations of cross-linker as it determines the overall structure of the MIP system. R increases switching from diethylene glycol diacrylate (DEGDA) (0.26 nm) to triethylene glycol dimethacrylate (TEGDMA) (0.28 nm) and polypropylene glycol dimethacrylate (PPGDMA) (0.30 nm) while swelling studies showed good correlation with these results. Using the same methodology, they showed that the separation efficiency of glucose MIPs might be potentially employed as a column supporting material for HPLC [4]. D-galactose and D-fructose were chosen as test molecules in order toevaluate the selectivity of glucose imprinted HEMA-based polymers. Columns filled with MIPs cross-linked with DEGDA (monomer:glucose 3:1, 5kGy) showed better separation comparing to other MIPs due to size of thecavity created for glucose.

Surface Imprinted Polymers

The functionalizationof polymer surfaces with molecular recognition capability gained attention due to the potential usage of molecularly imprinted polymersfor analytical applications [28]. The surface grafting methodology increases the accessibility of the target moleculeto the binding sites when compared to bulk polymerization. Nevertheless, activated surfaces that link the grafted layer are mostly necessary forsurface treatment. Radiation induced graft polymerisation can overcome this requirement by producing free radicals onto poorly reactive solid polymers.

Surface imprinted polymer particles were also explored by gamma irradiation. Uezu et al. reported that post irradiation of dysprosium ion imprinted polymer (IIP) particles resulted in a better separation for zinc by covalent approach [21,23-25]. Rao et al also reported a synthetic route of IIP particles for selective enrichment of uranyl ion from dilute aqueous and synthetic sea water solutions containing dysprosium ion from Y, Nd, La and Lu [29]. In the same work they found the selectivity of post irradiated (0.5 Mrad) styrene based IIP particles for Dy then comparedto unirradiated IIP particles by using liquid-liquid extraction [29]. TGA (thermal gravimetric analysis) results indicated that polymers kept their structural stability during the irradiation. The average pore diameters were in the range of 2-6 nm, indicating that the dysprosium ion leached. At the same time, the rigidity of the MIPs increases while the diameter is decreasing. The non-selectivity of blank polymer particles for dysprosium over other lanthanide ions and 35-180-fold enhancement in selectivity coefficients of irradiated dysprosium IIPs.

Wolman et al showed the potential use of radiation induced graft polymerization in a polar medium [29]. Bacitran A (Bac), a cyclic decapeptide, was chosen as a target molecule to synthesize MIP by grafting onto macroporous polyethylene membranes. Stable monomer-Bac complexes were obtained in aqueous solutions resulting from the interaction of copper(II) with histidine and vPy in polar environments. They investigated different stoichiometries of copper(II)-Bac and copper(II)-vPy complexes by following absorption spectra in the visible region. Imprinted graft polymerization was performed by immersing membranes in copper(II), Bac, vPy and DEGDMA solutions to allow self-assembly, followed by gamma radiation. They reported that MIPs had higher bacitracin adsorption capacity than non-imprinted polymers. Also, MIPs showed a 5-fold greater selectivity to bacitracin over chemically modified bacitracins [30].

Ranada et al. have synthesized MIPs for phloretic acid by grafting onto PE/PP non-woven fabrics [8]. The functional monomer N-vinyl imidazole (VIm) waschosen to imprint phloretic acid (p-hydroxyphenylpropionic acid, HPPA),

letting a strong interaction between the basic monomer and carboxylic acid groups of the template [31]. The authors explored parameters such as the irradiation dose, grafting effect and template molecule concentrations to design an efficient imprinting system. The grafting of MIP matrices onto PE/PP non-woven fabrics augmented while increasing the absorbed dose within the range of 60-160%. PAL spectroscopy results showed the effect of grafting on the free-volume hole radius comparing imprinted and non-imprinted polymers. Additionally, the diameter of the fabric together with the maximum grafting ratio was measured, followed by SEM analysis for further proof of imprinting. The binding properties of the proposed MIP grafted non-woven fabrics were followed by binding isotherms.

Conclusions and outlook

This review mainly focussed on the development of MIPs by using gamma radiation underlining the advantages of this technique over other approaches. The efficiency of imprinting is mainly affected by the template and functional monomer interactions, directly affected by temperature. We strongly believe that more studies on the advantages offered by radiation induced methodologies would be beneficial in the future.

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