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Molecularly imprinted polymer based enantioselective sensing devices: A review

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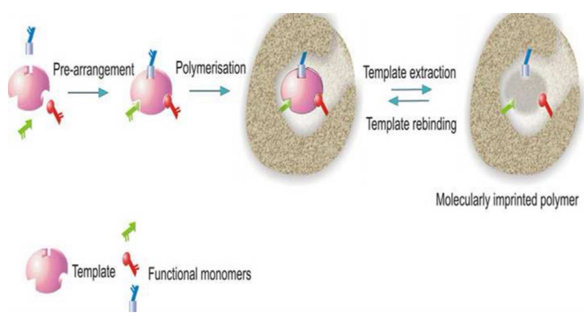
HIGHLIGHTS

- Impact of chirality has significant ramifications in many fields of economic interest.
- MIP provides a unique opportunity for the creation of 3-dimensional cavities.
- MIP-based chiral recognition sets an exotic trend in development of chiral sensors.
- We present about rational design of chiral sensors as selective and sensitive devices.

GRAPHICAL ABSTRACT



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ABSTRACT

Chiral recognition is the fundamental property of many biological molecules and is a quite important field in pharmaceutical analysis because of the pharmacologically different activities of enantiomers in living systems. Enantio-differentiating signal of the sensor requires specific interaction between the chiral compounds (one or a mixture of enantiomers) in question and the selector. This type of interaction is controlled normally by at least three binding centers, whose mutual arrangement and interacting characteristics with one of the enantiomers effectively control the selectivity of recognition. Molecular imprinting technology provides a unique opportunity for the creation of three-dimensional cavities with tailored recognition properties. Over the past decade, this field has expanded considerably across the variety of disciplines, leading to novel transduction approaches and many potential applications. The state-of-art of molecularly imprinted polymer-based chiral recognition might set an exotic trend toward the development of chiral sensors. The objective of this review is to provide comprehensive knowledge and information to all researchers who are interested in exploiting molecular imprinting technology toward the rational design of chiral sensors operating on different transduction principles, ranging from electrochemical to piezoelectric, being used for the detection of chiral compounds as they pose significant impact on the understanding of the origin of life and all processes that occur in living organisms.

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1. Introduction

Continuous assays of metabolic substances having the asymmetric carbons in their structures have significant impact on the understanding of the origin of life and all processes that occur in living organisms. Most of biochemical systems functioning in living organisms involve chiral interactions resulting from different stereochemistry of numerous biologically active compounds such as amino acids, sugars, peptides, proteins, and polysaccharides. The presence of chiral compounds in human biological fluids (serum, urine, and spinal fluids) as normal metabolites due to human metabolism or drug metabolism warrants an accurate methodology for monitoring level of these molecules in bio-fluids, since their higher or lower levels could be correlated as substantial indicative (marker) of functional abnormalities in human bodies.

A huge interest in chiral analysis emerges from the fact that the present pharmaceutical and chemical industries rely on the synthesis of enantiomeric components to the large extent. Although, these isomers do not possess any physical differences, they can have different influences on living organisms. As such it is most important to synthesize drug with particular ingredient of pure enantiomer. The fact, how the chiral purity is important for pharmaceutical industry, can be illustrated by the worldwide sale of chiral components as a racemate, which decreased from 35% in 1983 practically to zero in 2001. Thus, the prognosis of revenues from chiral technology now demonstrated over triple growth during past 10 years in the quest for pure chirals and predicted the involvement of 15 billions of dollars business [1].

Many examples, showing that enantiomers differ in bioactivity, rate of reaction or time of dissolution and each enantiomer manifests a different disease, can be found in the literature. So, it is very important to find analytical method that can discriminate between the D- and L-enantiomers. These methods should reveal reliable analytical information, fast analysis, and could be applicable for the continuous monitoring of enantiomers in biological fluids.

Separation and determination of enantiomers are currently being performed most commonly by chromatographic and electrochemical methods. However, the sampling process in enantioselective analysis may introduce a lot of uncertainties, especially when a separation method uses inadequate chiral selector [2]. Alternatively, the introduction of different types of enantioselective sensors and biosensors assure the reliability of the assay, as the enantiomers can be determined without prior separation, directly from the matrix, involving only dissolution and dilution steps [2–7].

Nature has attracted and inspired scientists for many years to develop chiral selectors with enhanced properties, akin to natural processes in nature. In this context, several kinds of chiral selectors viz., cyclodextrins (CDs), crown ethers, macro-cyclic antibodies, serum albumin, quinine/quinidine derivatives, and calf thymus DNA (ctDNA) have been fabricated. The paradigms of these 'intelligent' systems are of biological origin that could be exploited for chiral separations [8]. Although, biological receptors have specific molecular affinity and have widely been used in diagnostic bioassays and chemo/biosensors, they are often produced via complex protocols with a high cost and demand specific handling conditions because of poor stability. Moreover, the natural recognition elements for many analytes under investigation are often difficult to be procured [9–12]. One of the most burgeoning technologies of this century for the preparation of biomimetic materials is undoubtedly molecular imprinting. This is a most versatile technique to produce highly selective synthetic receptors and can, in principle, be applied to molecular structures (templates) spanning from small ions to large bio-macromolecules [10,12,13]. Simply put, the method involves the formation of molecular cavities in a synthetic polymer matrix that are complementary in terms of functional and structural characteristics to a template molecule/entity.

Now-a-days, the ability of molecularly imprinted polymers (MIPs) to selectively recognize and bind the template structure, in the presence of closely related chemical species, has made them of interest for use in quantitative discrimination of chiral molecules prevalent in real world samples. Furthermore, MIPs have obviously an edge over conventional chiral selectors in terms of the ease of preparation, scalability, low material cost, and flexibility. As a result, the molecular-imprinting approaches have extensively been exploited to produce target-specific chiral stationary phases (CSPs) for a broad range of chiral compounds [14,15] including amino acid derivatives [16], peptides [17], natural compounds, and a variety of drugs [14]. In general, MIP-based CSPs have excellent chiral recognition properties for the template (chiral) species and are endowed with the characteristics of high enantioselectivity, high substrate-specificity, and elution predictability. The added feature of these CSPs is their capability to discriminate, not only between enantiomers but also between structurally closely-related stereoisomers.

Although, in recent reviews [18–20], the diverse applications of MIPs for enantioselective recognition have been discussed emphasizing only capillary electrophoresis chromatography (CEC), high-performance liquid chromatography (HPLC), and other chromatographic techniques, a very limited account of enantioselective MIP-sensors were provided. We have also reported a monograph which presented a useful guide to researchers, exploiting MIP technology for potential applications in the development of nano-structured sensors as highly sensitive and selective medical devices [21], but this is not effective to provide much information about the enantioselective sensors. This review is meant to update MIP-researchers in the enantio-sensing field, highlighting important enantio-sensing methods hitherto contemplated for chiral discrimination and quantification, involving the specificity of MIP core shells featured in different shapes and textures.