Molecularly Imprinted Membranes for Separation

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Abstract: Among various studies on molecular imprinting, the application of molecular imprinting to membrane separation is still a novel study though the first application was reported in 1962. Molecular recognition sites introduced into polymeric membranes by applying molecular imprinting leads to enhancement of permselectivity. In membrane separation, not only permselectivity but also flux (throughput) is important factors. In membrane separation, it is hard to simultaneously enhance both factors. From this, it was revealed that nanofiber or molecularly imprinted nanofiber membranes had potential to enhance both key factors. In the present short review, the application of molecular imprinting to membrane separation will be briefly surveyed.

Keywords: Chiral separation, Membrane, Molecular imprinting, Permselectivity, Separation.

1. INTRODUCTION

Membrane separation has been gathering many attentions in these days, since separation with membrane is perceived to be an ecological, environmentally benign and economical separation technology [1-3]. Membrane transport phenomena consist of a couple of processes, such as incorporation of substrate into a membrane and diffusion of substrate within the membrane. Incorporation of substrate into a dense membrane is called solubility and that into a porous membrane partition. In other words, solubility and partition mean a kind of affinity between a given membrane and substrate. The latter is often called diffusivity. It is greatly dependent on the dimension and/or shape of substrate [4]. From this, the range of diffusivity is thought to be intrinsically limited. Contrary to diffusivity, affinity between the membrane and the substrate, which is so-called molecular recognition, is theoretically ranging from naught to infinity.

From above, introduction of molecular recognition sites into a membrane is a facile way to enhance permselectivity. In the present short review, the author described the potential of molecularly imprinted membranes in membrane separation.

2. MOLECULAR IMPRINTING

Molecular imprinting is one of facile ways to introduce molecular recognition sites into membranes with ease. Especially, adopting an alternative molecular imprinting, polymeric materials are directly converted into materials with molecular recognition sites, such as membranes, adsorbents, sensor chips and so forth. The origin of alternative molecular imprinting can be traced back to the pioneering study reported by Michaels and his colleagues in 1962 [5]. Bio-imprinting [6,7], in which the original recognition site in enzyme was modified by a print molecule, can be categorized as an extension of Michaels's study [5]. The scheme of alternative molecular imprinting is shown in Figure **1**. Contrary to conventional molecular imprinting proposed by Wulff and Sarhan in 1972 [8], as described previously, polymeric material is used instead of functional and cross-linkable monomers. From Figure **1**, materials with molecular recognition sites can be obtained without any laborious laboratory work by applying an alternative molecular imprinting. Anyone, who have never experienced chemical laboratory work, can prepare molecularly imprinted materials from polymers and print molecules. Applying an alternative molecular imprinting, various polymeric materials, such as synthetic polymers [9-11], oligopeptide derivatives [12-22], derivatives of natural polymer [23] and natural polymers [24] were directly converted into molecular recognition materials or membranes.

3. APPLICATION OF MOLECULAR IMPRINTING TO MEMBRANE SEPARATION

As mentioned above, the application of molecular imprinting to membrane separation was first reported by Michaels and his colleagues in 1962 [5]. Following their paper, they were stimulated by Dickey's study [25]. Pervaporation of xylene isomers was studied by polyethylene membranes conditioned by *p*-xylene. The membrane transported *p*-xylene over *o*- or *m*-xylene. Their study is the first application of molecular imprinting to membrane separation. In addition, their study is the first paper on alternative molecular imprinting. From above, Michaels' paper [5] is a

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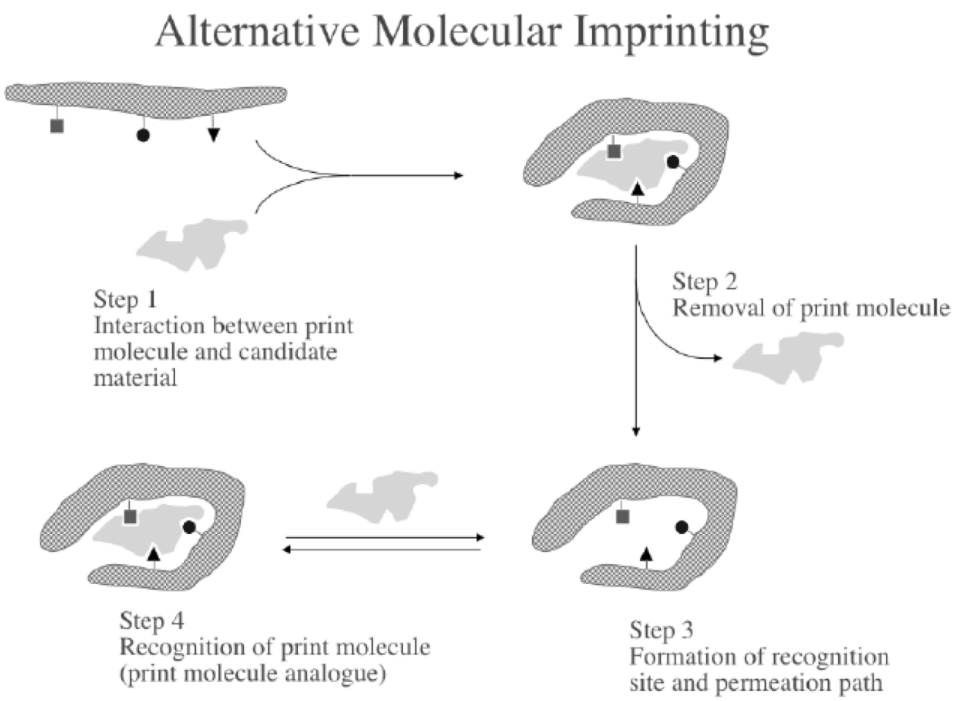
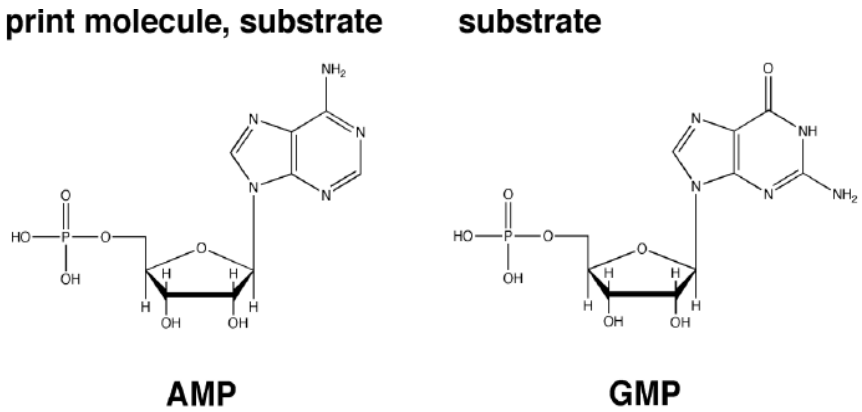


Figure 1: Schematic representation of alternative molecular imprinting.



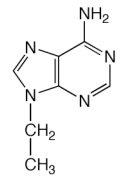
Scheme 1:

commemorable paper not only in molecular imprinting but also in membrane separation.

In 1990, molecularly imprinted membrane prepared by conventional molecular imprinting was reported [26]. In this study, non-covalent molecular imprinting was adopted as a conventional molecular imprinting. Non-covalent molecular imprinting, which is simpler than covalent molecular imprinting among conventional molecular imprinting, has been often adopted by many molecular imprinters since Arshady and Mosbach reported [27]. In their study, molecularly imprinted membranes were prepared by 2-(*N*,*N*-diethyl)-aminoethly methacrylate (DMAEMA) and ethylene-glycole dimethacrylate (EGDMA) in the presence of adenosine monophosphate (AMP) as a print molecule. AMP was selectively transported over guanosine monophosphate (GMP) by applying a potential difference as a driving force for membrane transport, since those substrates are charged ones.

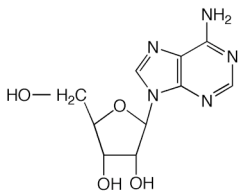
In membrane separation, the substrate less incorporated into membrane is often transported faster than the preferably incorporated one. Such membrane transport phenomena have been often observed. The interaction between membrane and permeant preferably incorporated into membrane is stronger than that between membrane and the less preferable one; as a result, the diffusivity of preferably incorporated substrate was retarded. This led to selective transport of less incorporated substrate. Especially, such membrane transport phenomena have been often

Print molecule:

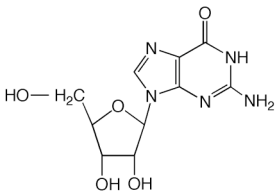


9-Ethyladenine (9-EA)

Substrates:



Adenosine (As)



Guanosine (Gs)

Scheme 2:

observed in chiral separation with molecularly imprinted membranes. The permselectivity reflecting its difference in affinity was realized by electrodialysis, which will be described later [16,17,20].

Competitive membrane transport was studied using the membrane prepared from methacrylic acid (MA) and EGDMA in the presence of 9-ethyladenine (9-EA) as a print molecule [28]. In this study, fortunately adenosine (As), which was preferably incorporated into the membrane, was selectively transported over guanosine (Gs) and the permselectivity of 3.4 was observed.

Membrane transports of bio-related substrates have been studied with molecularly imprinted membranes prepared by conventional molecular imprinting [29-31].

As described in the previous chapter, application of molecularly imprinted membranes prepared by an alternative molecular imprinting has been started with Michaels' study [5].

As an application of alternative molecular imprinting to membrane separation, optical resolution has been intensively studied since 1994 [12,13]. Chiral separation ability of molecularly imprinted membranes from oligopeptide derivatives was dependent on the absolute configuration of the print molecule and that of constituent amino acid residue (Figure **2**). In other words, the membrane consisting of oligopeptide residue from D-amino acid and imprinted by D-amino acid derivative recognized the D-enantiomer over the corresponding L-enantiomer and *vice versa* [20]. The results suggested that chiral recognition sites were constructed by racemic print molecule not by optically

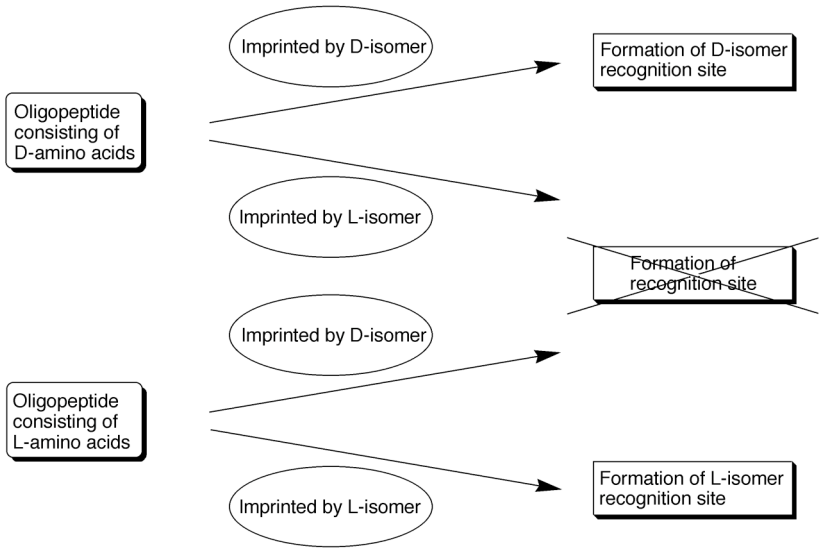


Figure 2: Summary of alternative molecularly imprinted membranes having oligopeptide as a chiral recognition site.

pure one, which was confirmed in this paper [20]. Among racemic print molecules, the print molecule with same absolute configuration of the consisting amino acid residue worked well as a print molecule, while antipode just worked as a porogen. The molecularly imprinted oligopeptide membranes recognized not only the print molecule analogue but also other α-amino acids, having same absolute configuration as that of print molecule [14,15].

Adopting concentration gradient as a driving force for membrane transport, the permselectivity was opposite to adsorption selectivity, which was due to a relatively strong interaction between membrane and substrate, of which absolute configuration was same as that of print molecule [14,16,17,20]. It was revealed that electrodialysis was one way to selectively transport enantiomer preferentially incorporated into the membrane [14,16,17,20].

A simultaneous transport of both enantiomers from a racemic mixture is an interesting and effective way to resolve racemates. Using both D- and L-enantiomer recognition membranes, "dual direction electrodialysis" was attained. In Figure **3**, dual direction electrodialysis of racemic mixture of Glu through two types of cellulose acetate membranes is shown [23]. Dual direction electrodialysis was also studied with carboxylated polysulfone [9] and oligopeptide derivative [20].

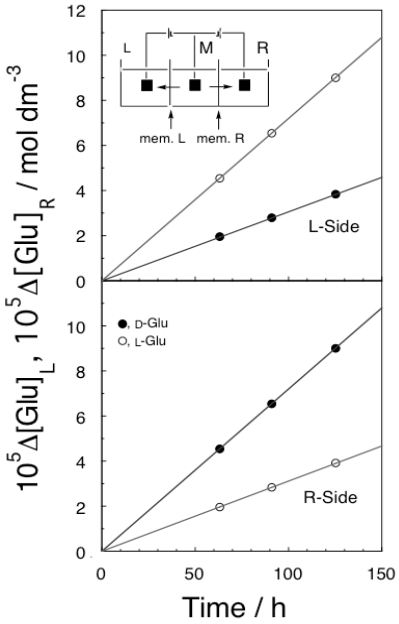


Figure 3: Chiral separation of racemic mixture of Glu through two types of molecularly imprinted cellulose acetate membrane by dual direction electrodialysis.

The factors affecting molecular recognition abilities, such as sequence and the amino acid residue content [18], number of amino acid derivative residue [21,22], and polarity of solution [19], where molecular recognition took place, were also investigated.

The effectiveness of alternative molecular imprinting has been confirmed by membranologists, such as Kobayashi *et al*. [32,33], Drioli and his colleagues [34,35], Ramamoorthy and Ulbricht [36], Cristallini and his coworkers [37], Jiang *et al*. [38], and Ul-Haq and Park [39].

4. MOLECULARLY IMPRINTED NANOFIBER MEMBRANES

As mentioned so far, enhancement of permeselectivity in membrane separation is easily attained by introduction of molecular recognition sites by applying molecular imprinting, such as conventional molecular imprinting or alternative molecular imprinting. In membrane separation, permselectivity and throughput (flux) are a couple of key factors. In a sense, enhancement of flux is more important than that of permselectivity. The enhancement of flux is indispensable so that molecularly imprinted membranes can be applicable in various industries.

A membrane form of nanofiber fabric was revealed to be a suitable to enhance throughput without a concurrent reduction in permselectivity [40-44], since permselectivity and throughput in membrane separation often show a trade-off relationship. The results revealed that flux values were one to two orders of magnitude enhanced without a concurrent reduction in permselectivity.

In addition to this, it was also revealed that the membrane form of nanofiber fabric itself is a suitable to attain better membrane performance [44].

At last, some references are listed [45-50] for the readers, who would like to deeply study molecular imprinting and/or application of molecular imprinting to membrane separation.

5. PERSPECTIVE

Molecular imprinting is the most applicable ways to obtain polymeric materials with molecular recognition sites. Among molecular imprinting, alternative molecular imprinting is a promising method to obtain separation membrane with molecular recognition site, since any polymeric materials are directly converted into molecularly imprinted membranes by applying the alternative molecular imprinting.

Membrane performances, such as permselectivity and flux, should be enhanced simultaneously so that membranes can be applicable in various industries. Even though simultaneous enhancement of both factors could not be attained, flux should be enhanced without a concurrent reduction in permselectivity by adopting nanofiber or molecularly imprinted nanofiber membranes.

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