Thermo-Responsive Membranes for Chiral Resolution

In this chapter, the design, fabrication and performance of thermo-responsive membranes for chiral resolution with a high performance are introduced. The membrane is designed with both chiral selectivity based on molecular recognition of beta-cyclodextrin ($\beta$-CD) and thermo-sensitivity based on phase transition of PNIPAM. Linear PNIPAM chains are grafted onto porous Nylon6 membrane substrates by using the plasma-graft pore-filling polymerization method, acting as micro-environmental adjustors for $\beta$-CD molecules. $\beta$-CD moieties are introduced into the linear PNIPAM chains by the chemical grafting polymerization method, acting as chiral selectors. The phase transition of grafted PNIPAM chains affects the micro-environment of $\beta$-CD molecules and then the association between $\beta$-CD and guest molecules. The chiral selectivity of the prepared thermo-responsive membranes in chiral resolution operated at a temperature below the LCST of PNIPAM is higher than that of membranes with no thermo-sensitivity, while the decomplexation ratio of enantiomer-loaded thermo-responsive membranes in decomplexation operated at a temperature above the LCST is much higher than that of membranes with no thermo-sensitivity. By simply changing the operating temperature, high selective chiral resolution and efficient membrane regeneration can be achieved.

5.1 Introduction

Chiral recognition of molecules plays an important role in the biological processes.\cite{1,2} Different enantiomers of a chiral drug usually exhibit different pharmacological activities, metabolic effects, metabolic rates and toxicities due to the high degree of stereoselectivity of enzymatic reactions and other biological processes.\cite{3,4} Therefore, drugs have to be applied in an optically pure form to prevent unwanted
side effects or even toxicity. In the last two decades, enantioseparation technology has been developed rapidly in response to the demand for optically pure compounds in a wide variety of applications.\textsuperscript{[4]} Membrane technology, because of its high efficiency, low energy usage, simplicity and continuous operability, has been considered as the most potential method for large-scale enantioseparation processes.\textsuperscript{[1,4-6]} Consequently, much attention has been drawn to chiral membrane technology. It is well known that enantioselective solid membranes, which can fulfill the demand for industrial applications,\textsuperscript{[1,7]} are more stable and stronger than liquid membranes.

Generally, enantioselective solid membranes can be classified into two categories, \textit{i.e.}, diffusion-selective membranes and adsorption-selective membranes. A diffusion-selective membrane is considered to be a membrane with no specific chiral selectors for the chiral interaction, but consists of a chiral polymer which can either be coated on a non-chiral support layer or can be self-supporting.\textsuperscript{[1,8-12]} The main disadvantage of diffusion-selective membranes is the reverse relationship between selectivity and flux, which has hindered industrial-scale applications of diffusion-enantioselective membranes. Sorption-selective membranes mainly make use of a chiral selector embedded in a polymer matrix, and these selectors are known from analytical separation methods and form a one-to-one complex with enantiomers by means of specific molecular interaction.\textsuperscript{[1,13-17]} Unlike diffusion-enantioselective membranes, an adsorption-enantioselective membrane can enhance the flux and selectivity simultaneously, which is the most promising approach for achieving high flux and selectivity as well as high efficiency and stability. This makes it applicable in industrial-scale chiral resolution processes. However, previous investigations focused mainly on the enhancement of flux and selectivity, no research was carried out on the improvement in regeneration of enantiomer-loaded membranes. It is a recognized fact that efficient regeneration of saturated membranes for re-use could greatly reduce the costs resulting from the consumption of raw materials and disposal of membranes.

Recently, the author’s group reported on a novel thermo-responsive membrane for chiral resolution, which featured a simple and efficient process for membrane regeneration.\textsuperscript{[18]} The proposed membrane simultaneously exhibited chiral selectivity based on molecular recognition of beta-cyclodextrin (\(\beta\)-CD) and temperature sensitivity based on phase transition of poly(\(N\)-isopropylacrylamide) (PNIPAM). By simply changing the operating temperature, chiral resolution with high selectivity and efficient membrane regeneration was achieved.

\section*{5.2 Concept and Design of the Thermo-Responsive Membrane for Chiral Resolution}

The concept of the thermo-responsive membrane for chiral resolution is schematically