Star Shaped Molecularly Imprinted Polymer Working as a Drug Carrier

Tomonori Nakayama, Tadashi Yamagishi, Shin-ichi Sekine, Yasuo Yoshimi
Shibaura Institute of Technology, Tokyo, JAPAN

1. INTRODUCTION

Carrier-assisted liquid membrane method is very promising for simple and highly selective separation process[1]. The carrier must bind with the target molecule and dissolved in the liquid membrane phase, so is very difficult to synthesize. Contrastively, molecularly imprinted polymer (MIP) is relatively easy to synthesize.

Star polymer is colloidal particle which has "arm" domain for high affinity with solvent and crosslinked "core'' domain. We designed a star polymer whose core is imprinted by template. We also designed a novel liquid membrane process using the star shaped MIP as a carrier. In this work, the star shaped MIP of L-phenylalanine (PA) was synthesized using living radical polymerization. The ability of the polymer as a carrier was estimated by observing transport of the template through experimental method of bulk liquid membrane.

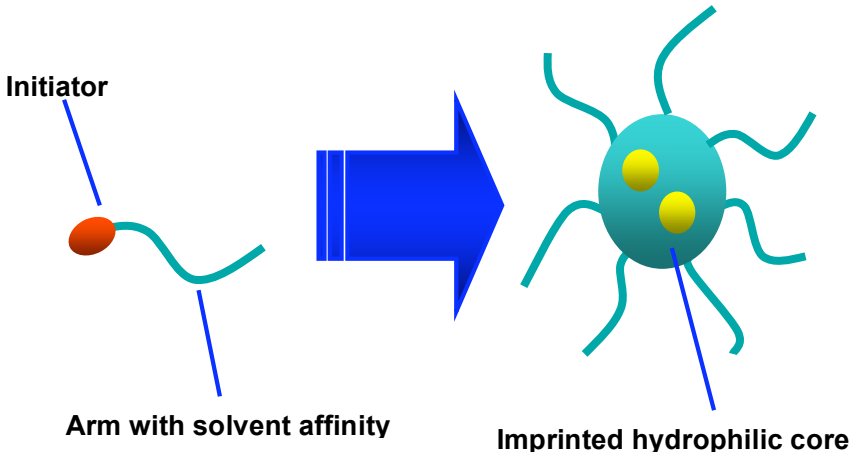

Fig.1: Molecularly imprinted star polymer (StarMIP)

2. MATERIALS AND METHODS

Living radical polymerization of methyl methacrylate (MMA) was allowed to occur by using initiator of benzyl diethyldithiocarbamate under ultraviolet (UV) irradiation. The arm polymer was obtained after reprecipitation in dimethyl ether. The star shaped MIP was synthesized through photo-copolymerization of acrylamide, *N,N*-methylenebisacrylamide, and methacrylic acid with PA as a template by the arm polymer as an initiator in emulsified solvent of chloroform and water (5:1 V/V). StarMIP was repricipitated in methanol. The prepared polymer is referred to as StarMIP. StarNonMIP was also synthesized by the same procedure in the absence of the template.

The transportability for PA of the StarMIP and StarNonMIP was estimated by

bulk liquid membranes using U-shaped glass tube. Three phases for the aqueous source of the PA, chloroformic liquid membrane with the star polymer, and the aqueous receiving of PA were formed in the tube. Time courses of PA concentrations in the source phase and the receiving phase were observed.

3. RESULTS AND DISCUSSION

3-1 Characterization of the StarMIP

The all synthesized polymer can be dissolved in chloroform stably. The molecular weight of the arm polymer was estimated to be 28,000 by the size exclusion chromatography. The diameter of the StarMIP and StrarNonMIP was determined approximately 200 nm by light scattering spectroscopy.

The NMR spectra of StarMIP and arm polymer were almost same as shown in **Fig.2**. The result shows that the movement of the domain of poly MMA is free but that of the domain of poly acrylamide or poly methylene bis acrylamide is strictly limited[2]. Those results show that star-shaped polymer is synthesized by the oroginal procedure.

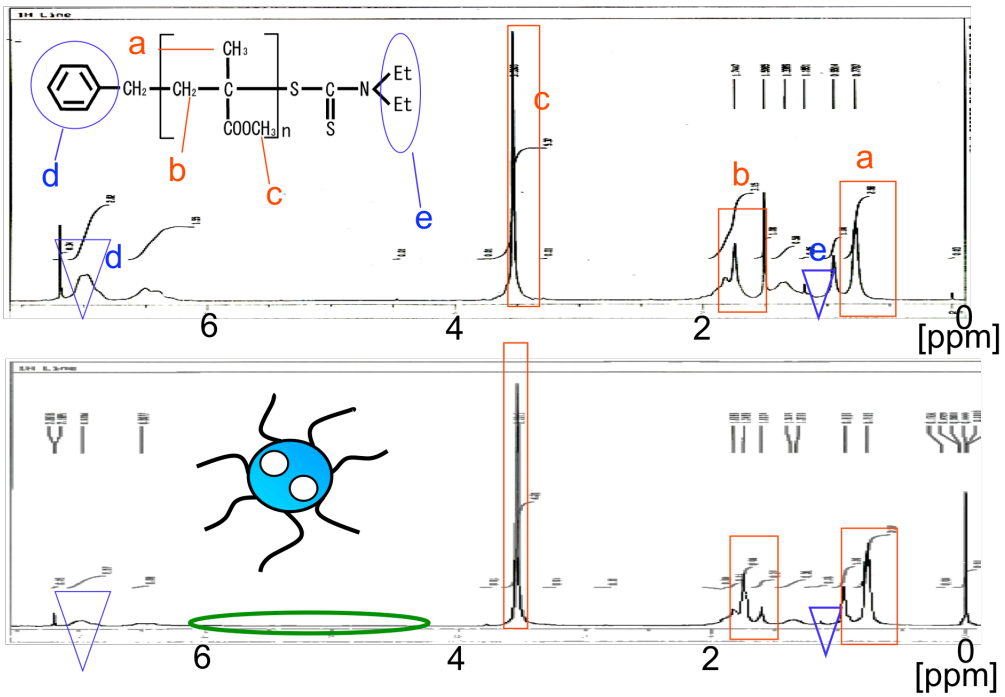

Fig. 2: Proton NMR spectra of the arm polymer (upper) and StarMIP (lower).

3-2. Bulk liquid membrane experiment

The PA concentration in the receiving phase increased slowly in the experiment with the StarMIP during 120 hr operation of the liquid membrane experiment. Contrastively, PA was not detected at all in the receiving phase of the experiment with StarNonMIP throughout the operation.

Those results suggest that the star-shaped molecularly imprinted polymer can work as a carrier of the liquid membrane process. However, less than 3 % of the template PA was transported for 120 hr. The transportability is too low to apply the

StarMIP as a carrier in the industrial separation process. The results may indicate that the star MIP is rather suitable for drug delivery system for extremely slow administration.

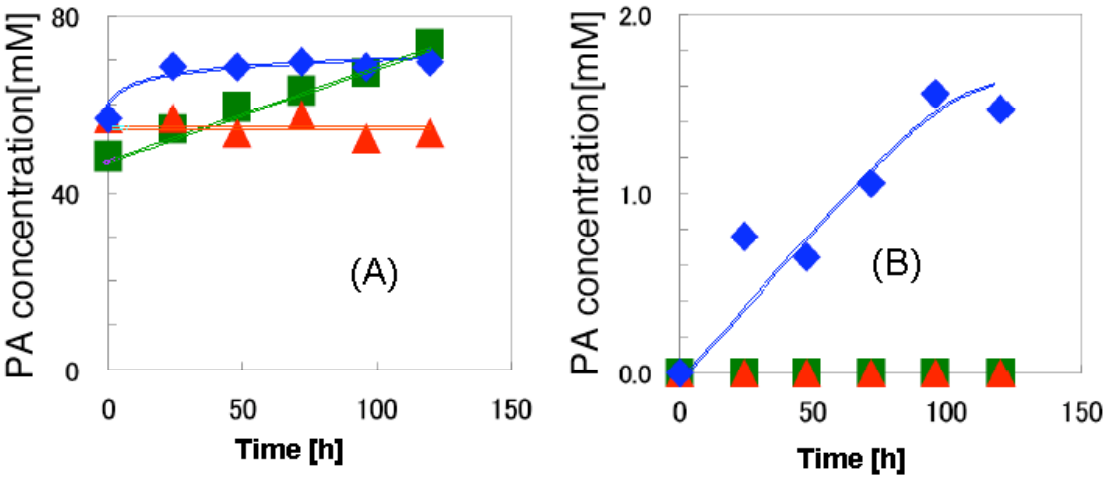

Fig. 3: Time course of (A) source phase and (B) receiving phase during liquid phase experiment with presence of StarMIP(diamond), StarNonMIP (square), and none (triangle) in the liquid phase.

REFERENCES

1. Chrisstoffels, L.A.J., Jong, F., and Reinhoudt, D.N. (1996), "Mechanistic Studies of Carrier-Mediated Transport Through Supported Liquid Membranes" In *Chemical Separations with liquid membranes: ACS symposium Series 642*, ACS, Washington DC, USA, pp. 18-56.
2. Baek, K.-Y., Kamigaito M., and Sawamoto M. (2001), "Core-Functionalized Star Polymer by Transition Metal-Catalyzed Living Radical Polymerization. 1. Synthesis and Characterization of Star Polymers with PMMA Arms and Amide Cores", *Macromolecules*, **34**, 7629-7635.

ACKNOWLEGMENTS

We thank Prof. Sergey A. Piletsky (Institute of BioScience and Technology, Cranfield University, Silsoe, UK) for fruitful discussion about the liquid membrane with liquid membrane. We also appreciate Dr. Toshio Shibno (National Institute of Advanced Institute of Science and Technology, Tsukuba, Japan) for discussion about design of the whole experiment. We thank Mr. Tsuneyoshi Torii (Sysmex Co., Ltd., Kobe, Japan) who performed light scattering spectroscopy. Y.Y. is grateful to the Ministry of Education, Culture and Sports, Science and Technology, Japan for the partial support of this work by the Grant-in-Aid for Scientific Research (No. 15710095).