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Stable surface coating of silicone elastomer with phosphorylcholine and organosilane copolymer with cross-linking for repelling proteins

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ABSTRACT

Poly(dimethylsiloxane) (PDMS)-based polymers are widely used in blood-contacting medical devices. However, the hydrophobic property causes adsorption of plasma proteins and activates blood clotting. There are several techniques for PDMS surface modification. However, the efficacy is limited to short duration due to the low glass transition temperature of PDMS. The goal of this study is to fabricate a highly stable polymer membrane with blood-compatibility on PDMS. Here, we synthesized random copolymer of 2-methacryloyloxyethyl phosphorylcholine (MPC), 3-methacryloxypropyl trimethoxysilane (MPTMSi) and 3-(methacryloyloxy) propyl-tris(trimethylsilyloxy) silane (MPTSSi). These copolymers are covalently and physically immobilized on PDMS surface by silane coupling (cross-linking) and hydrophobic interaction. Protein adsorption was significantly reduced on MPC copolymer-coated PDMS surface. In particular, copolymer containing 50% MPC unit was the most effective and maintained the effect for the longest duration (84 days). From analyses of X-ray reflectometry (XRR) and X-ray photoelectron spectroscopy (XPS), it is determined that the density of the polymer membrane is an important factor for the long-term stability. In addition, the coating of PDMS with MPC copolymer does not influence on oxygen permeability.

1. Introduction

Silicones, such as PDMS have been used for various medical devices because they are relatively non-toxic, thermally and chemically stable, and highly gas permeable [1]. In particular, silicone-based materials have been applied to peritoneal dialysis (PD), catheter and artificial heart lung apparatus [2]. Recently, it was reported that silicone-based cardiorespiratory devices were effective in percutaneous cardio pulmonary support (PCPS) and extracorporeal membrane oxygenation (ECMO) systems [3]. The devices were also clinically used in clinical for influenza A (H1N1) related acute respiratory distress syndrome (ARDS) [4]. However, since the surface of silicone is hydrophobic, there are unfavorable reactions, such as blood-clotting, protein adsorption, platelet aggregation and clotting when fresh blood comes in contact with the surface. In fact, when PDMS-based medical devices were used for an extended time, serious problems were reported, such as intratubular obstruction with thrombus and device failures [5].

Some studies have reported methods to improve the blood compatibility of PDMS by means of oxygen plasma treatment or ultraviolet light treatment [6,7], physical treatment [8] and chemical grafting [9]. Also poly(ethylene glycol) (PEG) brush-modified PDMS improved the blood compatibility [10]. However, the efficacy of these approaches is limited to a short time period (up to around 14 days). This is because hydrophobic recovery occurs due to the low glass transition temperature of the silicone, resulting in the re-construction and migration of the hydrophobic bulk silicone segments and the surface-coated/grafted polymers [11].

In this study, we aimed to fabricate a polymer for the silicone surface modifications to improve its biocompatibility for the long-term use (*e.g.* more than one month). In order to achieve this purpose, we designed random copolymers composed of MPC, MPTMSi and MPTSSi (Fig. 1A). Ishihara, et al. already demonstrated the high hemocompatibility of MPC copolymers, which could suppress non-specific protein adsorption [12]. And the PDMS surface coated with MPC polymers by chemical grafting were also reported [13,14]. We also, previously, reported co-polymers of MPC and MPTSSi, which have high affinity for PDMS surfaces (Fig. 1B) [15,16]. However, these approaches could not overcome the problem of polymer reconfiguration due to hydrophobic recovery. Here, in order to resolve the issue, we synthesized the random poly(MPC-*co*-MPSSi-*co*-MPTMSi). It is expected that the hydrophobic interactions of MPTSSi unit and the cross-linking of MPTMSi unit are effective to stabilize the membrane structure on the PDMS sur-

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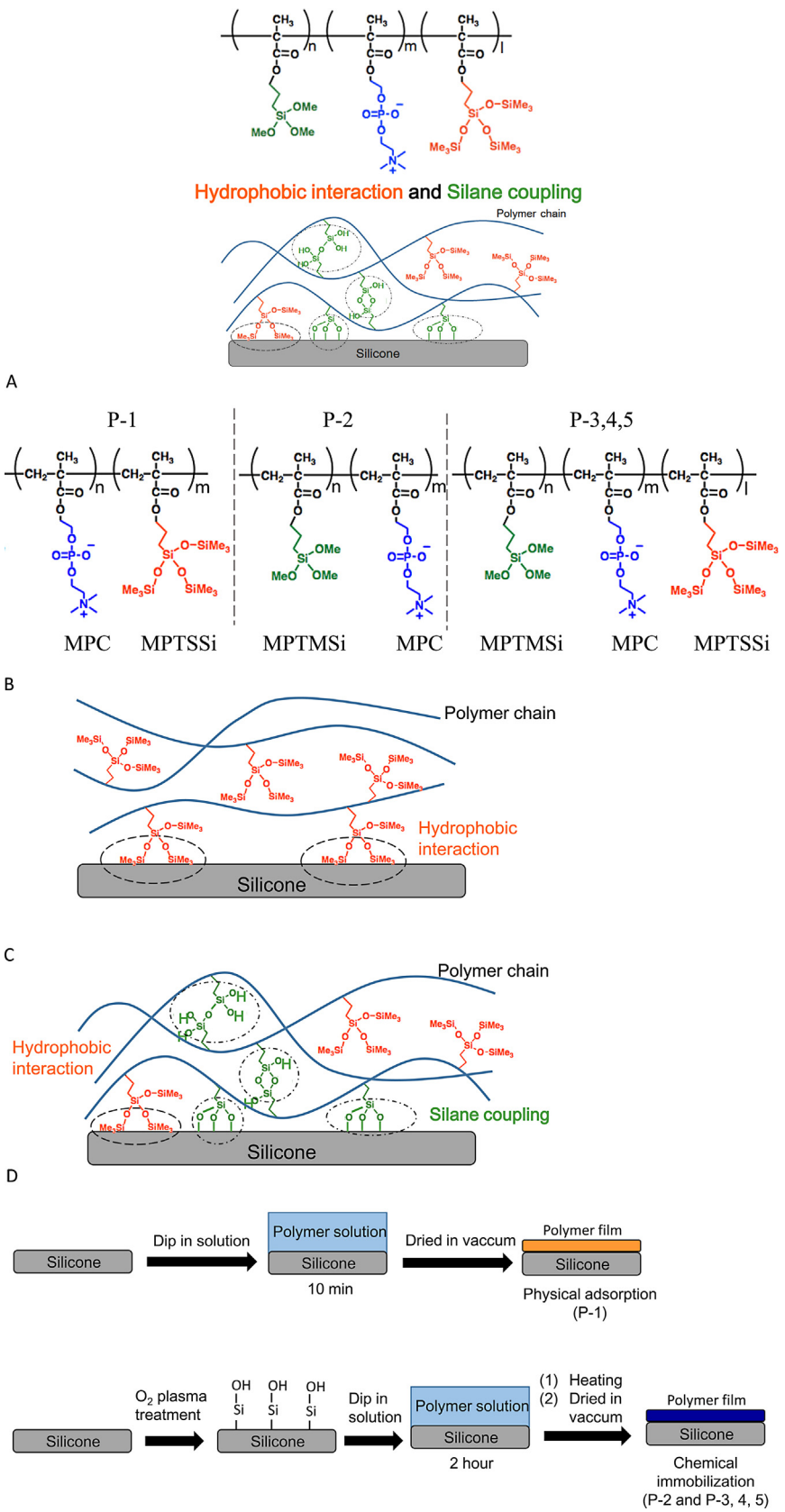

Fig. 1. (A) Chemical structure of random copolymers. (B) and (C) Schematic illustration of silicone surface modification with random copolymers ((B) P-1, (C) P-3–P-5). (D) Scheme of silicone surface modification with random polymers.