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論　文　内　容　要　旨

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学位論文題目	Preparation of biocompatible surface using phospholipid analogue polymer (リン脂質類似ポリマーを用いた生体適合性表面の作製)		

内容要旨

With the development of medical science and technology, medical implants and devices have become an indispensable part of medical care for some people. Various medical materials, such as contact lenses, catheters, stents, etc., are used or implanted in the human body. Correspondingly, as an implantable material, it also induces physiological responses in vivo. Nonspecific adsorption of proteins on surfaces is an essential problem for nanodrug carriers and medical implant materials. Recently, poly-zwitterionic materials have been shown to have excellent non-fouling properties and biocompatibility, which are inseparable from their strong hydration capacity and excellent biomimetic structure. Therefore, the biomedical applications of these zwitterionic materials have become one of the research hotspots.

2-methylacryloxyethyl phosphocholine (MPC) is a typical zwitterionic monomer containing cationic and anionic groups. MPC can form a hydration layer, resist the adsorption of non-specific proteins, and effectively maintain the natural conformation of proteins, which has been widely used. However, the environment inside the body is normally in the neutral range, but it is known that the local environment can be below pH 4 and in some cases under pH 3 due to cancer and inflammation, etc. When the pH is changed from alkaline to neutral, the uptake of fibrinogen by membranes with PC groups increases by about 40%, as the PC on the surface is not fully zwitterionic due to protonation. In addition, materials with PC groups have been reported to be positively charged in the acidic range below pH 4. In general, positively charged surfaces are expected to be less biocompatible, as they are less likely to inhibit adsorption of proteins and other clot-forming substances.

A novel zwitterionic monomer has been prepared in our previous report, 2-methacryloyloxyethyl cholinephosphate(MCP), which has a polar group structure opposite to that of MPC. The CP group has a terminal phosphate group and two desorption protons compared to conventional zwitterions. Therefore, it is expected to have properties different from those of conventional zwitterionic monomers that can inhibit protein adsorption at different pH ranges. In this work, MCP monomer was used for different surface modification methods to form the non-fouling surfaces. The main contents and conclusions of the study are as follows:

1. MCP was used to modify the glass surface via surface-initiated activators regenerated by electron transfer atom transfer radical polymerization (SI-ARGET-ATRP) to form the polymer brush on the glass surface. MPC also used the same preparation method to modify the glass surface as a comparison group. The surface hydrophilicity and non-fouling property were measured in different pH ranges. The results show that the

MCP-modified glass surface has the lowest water contact angle and can maintain a high hydrophilicity under acidic conditions, while the MPC-modified surface decreases hydrophilicity under acidic conditions. The protein adsorption test for non-fouling property also gave the similar result. Both MCP and MPC modified surfaces exhibit low protein adsorption level in the neutral environment. However, MPC showed a significant increase in protein adsorption in acidic environments, while MCP was still effective in avoiding protein adsorption. This indicates that MCP can be applied in a wider pH range than MPC.

2. MCP was also used to prepare block copolymers with butyl methacrylate (BMA), and p (MCP-co-BMA) copolymer modified polypropylene (PP) films were prepared by hydrophobic interaction between the BMA in the copolymer chain and PP film. The copolymer was prepared in different ratios of the MCP and BMA fractions to find a suitable ratio that would maintain both anchoring stability and biocompatibility. The durability test results showed that when the chain length of BMA increased, the stability of the anchoring also increased. But at the same time, the protein adsorption test showed the biocompatibility decreased significantly. While the ratio between MCP and BMA is 2 to 8, the copolymer coating can remain stable and resist protein adsorption.