論文の内容の要旨

Preparation of molecular composite using supercritical carbon dioxide and their application and function for biomaterials
(超臨界二酸化炭素を用いた分子複合体の調製と生体材料への応用とその機能)

星 徹

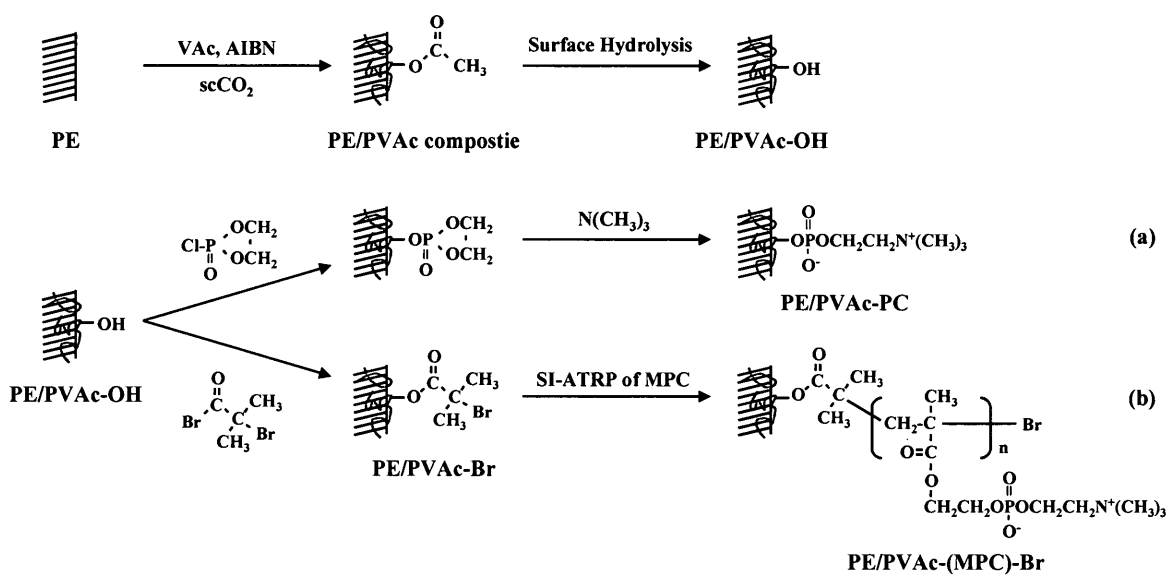
The basic point of this research is to control the bulk and surface properties of a polymeric material. Most biomaterials are modified with biocompatible polymers, gaining biocompatible surface for medical applications, such as the coating, grafting, or reacting of biocompatible polymers with the surface of substrates. Other methods include blending of the biocompatibility polymer with the substrate. In the above-mentioned methods, the surface properties can be controlled although the mechanical properties are hardly changed since they retain the properties of industrial substrate that does not adapt to tissues and organs. However, the difference in mechanical properties between a living system and artificial organs induces stress concentration near the anastomoses and interface, causing further undesirable responses such as thrombus formation and neointimal hyperplasia.

Polyolefins such as polyethylene (PE) is a conventional polymer and is very inert chemically; no harmful chemicals are produced even when it is burned. The mechanical properties of PE are good, and can be changed depending on the crystallinity. Also, various mechanical characteristics are expected of PE by copolymerization of ethylene and different monomer. Therefore, if the biocompatibility of PE could be improved without loss of its mechanical properties and processability, application of modified-PE would be used much more for biomaterials. The improvement of the bulk and the surface property of polyolefines is very difficult due to the disadvantage such as low surface energy, lack of chemical functionalities, difficulty to dye, poor hydrophilicity, and poor compatibility with synthetic polar polymers. In new preparation method for the molecular composite using supercritical carbon dioxide (scCO_2), various new materials can be created changing the following conditions such as the change in content rate of blending polymer and the kind of polyolefin and blending polymer. Also, mechanical properties of these materials can be controlled according to the above-mentioned condition.

The biocompatibility of molecular composite that controlled the mechanical properties is strongly required to be improved. The phosphorylcholine (PC) group and the 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer acts as a distinctive surface modifier. Surface with PC group modification is biomembrane-like surface based on the chemical structure of a phospholipid polar group and exhibits better biocompatibility than existing so-called biomaterials. Therefore, the molecular composite formation method using scCO_2 and its surface modification for PC-surface can control both the bulk and the surface properties and can expect to create novel polymer biomaterials.

In addition, $scCO_2$ have many unique properties such as low viscosity and near-zero surface tension. The surface modification of the part like the inner surface of the very narrow tube that is difficult in conventional methods such as photoinduced graft polymerization, surface-initiated radical polymerization, and polymer blend method is expected using $scCO_2$. The synthetic method using $scCO_2$ in this research may be lead to diverse functionalities of the molded polymer materials for biomaterials.

The solubility of a polar molecule in $scCO_2$ is considerably lower than that of a non-polar molecule, and thus, it is difficult to directly impregnate MPC monomer due to the presence of the polar PC groups. Biomaterials might possibly be prepared as polymer composite with a biocompatible surface by the use of the following two-step processes: (i) the first step would be to prepare polymer composite comprising polyolefin and hydrophobic polymer with reactiveness side chain using $scCO_2$ method and (ii) the second step would be to introduce PC groups onto the surface of molecular composite by surface reaction. Based on this hypothesis, this thesis attempts to create new polymeric materials that control the bulk and surface properties for biomaterials. Figure shows the procedure for developing the molecular composite with the biocompatible surface.



Chapter 2 demonstrates the preparation of molecular composite. The molecular composite comprising PE and poly(vinyl acetate) (PVAc) can be prepared by polymerization of vinyl acetate (VAc) in $scCO_2$ method. The solubility of the vinyl acetate of the hydrophobic monomer in $scCO_2$ is higher than that of the hydrophilic monomer such as MPC and HEMA. VAc may be impregnated into the PE substrate easily by $scCO_2$. Microstructure and mechanical properties of obtained material is evaluated. PE and PVAc were blended at the nanometer level. PVAc generated in the amorphous regions at nanometer level affected significantly the viscoelasticity and mechanical properties of PE/PVAc composite. The structure control in the direction of depth is possible according to the control of the mass gain. The molecular composite formation method using $scCO_2$ suggests that a modification only of the surface of substrate or a material with new function can be created.

In Chapter 3, the acetyl group on the surface of the PE/PVAc composite is converted to hydroxyl groups by surface hydrolysis. The hydroxyl group is the reaction site for the immobilization of the PC groups. The effect of surface hydrolysis to microstructure and mechanical properties is evaluated. PVAc of PE/PVAc composite was hydrolyzed from the surface to the depth of 40 ~ 80 μm. Also, in the lower than the melting temperature of the crystalline, the bulk properties of PE/PVAc composite are not affected because there is no structural alteration by the surface modification. Therefore, the surface hydrolysis doesn't affect the microstructure and mechanical properties of PE/PVAc-OH.

Chapter 4 and 5 demonstrates that the biocompatible surface is assembled by two different procedures of the introduction of PC group. A two-dimensional (2D) modification like the direct introduction of PC groups (Figure (a)) that describes in Chapter 4 and a three-dimensional (3D) modification like surface-initiated atom transfer radical polymerization (SI-ATRP) of MPC (Figure (b)) that describes in Chapter 5. The effect of surface morphology to surface properties such as protein adsorption and wettability is evaluated. the biocompatible surface could be assembled from the direct introduction of phosphorylcholine (PC) group or Surface-initiated atom transfer radical polymerization (SI-ATRP) of 2-methacryloyloxyethyl phosphorylcholine (MPC) without an adverse effect on the bulk properties because reaction temperature is the lower than the melting temperature of the crystalline of PE. Surface with PC modification prevented plasma protein adsorption effectively. The subsequent events of protein adsorption, including thrombus formation, the foreign body reaction, bacterial infection, and other undesirable responses do not occur.

The author of this thesis conclude that the present process for preparing protein adsorption resistant surfaces on molecular composites the introducing PC groups will provide an excellent method for developing new biomedical devices.

Moreover, in Chapter 6, the molecular composite formation method using $scCO_2$ and its surface modification were applied to molded polymer materials such as tube. The immobilization of PVAc and the surface hydrolysis were uniformly conducted as for both the inner surface and the outer surface. The biocompatible surface was assembled by the silane coupling reaction of PMSi that is MPC polymer with silane coupling agent on the surface of the tubular PE/PVAc-OH. The surface with PMSi modification shows a remarkable ability to suppress the protein adsorption and the high hydrophilicity. The use of surface modification that demonstrated in this thesis could lead to diverse functionalities of the molded polymer materials.

Also, this reaction procedure may be applicable to introduce various functional groups using other acid chloride compounds. The author concludes that the surface modification of PE after blending with PVAc is a promising procedure for synthesizing new polymer materials for other technical fields.