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Visible Light-Induced Novel Surface Modification Technique For Fabricated Devices

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This study describes a novel surface graft polymerization method providing durable layering of hydrophilic polymers on the material of fabricated devices, which was induced by visible light irradiation. First, dodecane end-capped with camphorquinone, which can initiate radical polymerization upon visible light irradiation, was impregnated into one face of the surface of a substrate such as segmented polyurethane film and poly(vinyl chloride) tube by coating. The treated surface was irradiated from the non-impregnated surface side in an aqueous solution of *N,N*-dimethylacrylamide. X-ray photoelectron spectroscopic analysis and water contact angle measurement of the film surface before and after irradiation provided evidence that a polymerized layer was produced and tightly fixed on the camphorquinone-impregnated surface even after thorough washing with water. Confocal laser fluorescence microscopic observations after staining with a fluorescence dye showed that the thickness of the produced polymer layer increased with irradiation time. The treated surface extensively prolonged whole blood coagulation time. This photochemical surface technology was applied for conferring potent biocompatibility to the inner surface of a fabricated artificial heart.

Key words: Surface Modification, Visible Light, Graft Polymerization, Camphorquinone, Device

1. Introduvtion

Since advanced medical devices such as an artificial heart is composed of different parts, each of which is made of different material, surface modification technology for assembled or fabricated whole body of device especially including blood-contacting inner surface has been long demanded. The development of surface modification method providing biocompatibility to fabricated medical devices is essentially required for highly reliable implant devices.[1-3] Previously, we developed ultraviolet light (UV) induced surface modification method[4-6], which has some drawback or limitations. For example, most polymeric materials absorb the UV light. Therefore, modification of an inner surface of the devices requires the direct irradiation to the region to be modified using an optical fiber delivered to the inside of the device (Fig. 1a).

A more practical approach is to develop a visible light-induced surface modification which has more versatile applicability as follows. Since visible light can pass through even thick polymeric materials, an inner surface of devices can be modified by irradiation from outer side of the device (Fig. 1b). In addition, the whole body of the device can be modified at the same time by enhancement with a field of light.

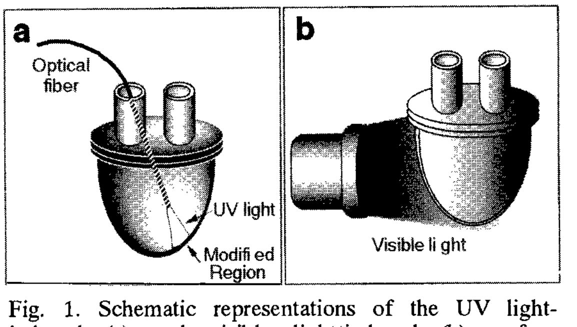

Fig. 1. Schematic representations of the UV light-induced (a) and visible light-induced (b) surface modifications of the inner side of a blood pump.

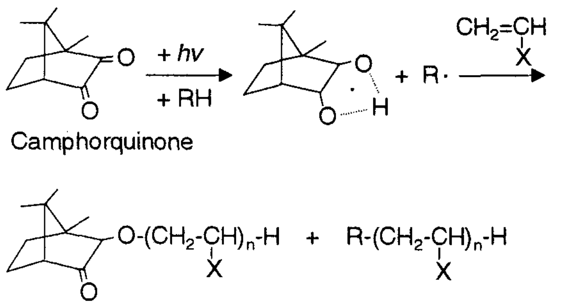

Fig. 2. Reaction schemes of photoinduced radical generating reaction of camphorquinone and subsequent polymerization reaction of vinyl monomers.

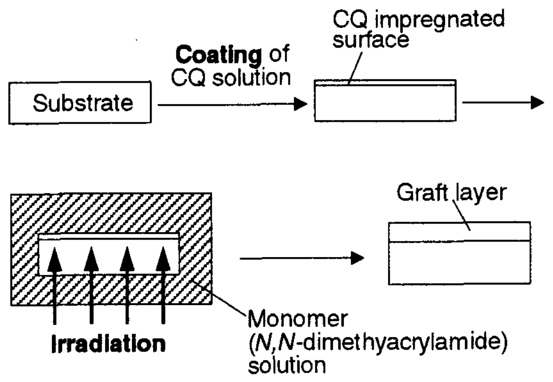

Fig. 3. Principle of the visible light-induced surface photopolymerization.

In this article, we report the development of a visible light induced novel surface graft polymerization method providing a durable hydrophilic polymer layering. The example is given to a ventricular assist device.

2. MATERIALS AND MATHODS

2.1 General Methods

A halogen lamp (Power Light, Tokuso, Tokyo, and VL-501, LPL Co., Ltd., Tokyo, Japan) was used as a light source. The chemical composition of the outermost surface layer was determined by x-ray photoelectron spectroscopy (XPS) with ESCA 750 (Shimadzu, Kyoto, Japan). The wettability of treated surfaces was evaluated by water contact angle measurements using the sessile drop method with a contact angle meter (Kyowa Kaimen Kagaku Co., Ltd., Tokyo, Japan). Thickness of graft copolymer layer was measured by confocal laser scanning fluorescence microscopic (Bio-Rad, Herfordshire, England) observations after staining with rose bengal.

2.2 Materials

Camphorquinone-derivatized dodecane was synthesized from 1,12-dodecanediol, which was purchased from Wako Pure Chemical Ind. Ltd. (Osaka, Japan) and acid chloride of carboxylated camphorquinone ((1S)-7,7-dimethyl-2,3-dioxobicyclo [2.2.1]hepyane-1-carboxylic acid) which was prepared and supplied by T. Mukai. *N,N*-Dimethylacrylamide (DMAAm) and solvents were obtained from Wako. A segmented polyurethane (SPU) film and a poly(vinyl chloride) (PVC) tube was purchased from Shidam Co., Ltd. (Tokyo, Japan) and Chubu Co., Ltd. (Nagoya, Japan), respectively.

2.3 Surface Polymerization

Surface polymerization was performed on SPU film and PVC tube, whose surfaces were impregnated with the camphorquinone-derivatized dodecane, by photoirradiation into an aqueous DMAAm solution (monomer concentration: 5 mol/dm^3) with a halogen lamp (light intensity: 100 mW/cm^2).

Table 1. Chemical compositions and water contact angles of photopolymerized surface

Surface	Elemental ratio[a]		Contact angle (degree)[b]	
	N/C	O/C	Adv.	Rec.
SPU film (substrate)	0.25	0.037	86.3	49.5
after photoirradiation	0.26	0.033	85.7	47.3
CQ[c]-impregnated film	0.15	0.022	88.5	58.7
after photoirradiation	0.18 (0.20)[d]	0.13 (0.20)[d]	42.7	~ 5

[a] Values as obtained by XPS measurements.
[b] Measured by the sessile drop method.
[c] CQ means camphorquinone-derivatized dodecane.
[d] Parentheses show theoretical values of polyDMAAm.

3. RESULTS AND DISCUSSION

3.1 Surface Modification

The visible light-induced surface modification method is based on photochemistry of camphorquinone. Upon visible light irradiation (wavelength: 400 - 500 nm), camphorquinone generates radicals by protonation (Fig. 2).[7,8] The generated radical can initiate radical polymerization of vinyl monomers.

A schematic diagram of the sequence of the preparation method of a surface polymerization on a polymer substrate is illustrated in Fig. 3. At first, a methanol solution containing camphorquinone-both-end-capped dodecane was cast on substrates such as SPU film and PVC tube. After air-dried, the coated substrate was subjected to immersion into DMAAm solution and subsequent irradiation with visible light through the substrate.

The surface compositional characterization of the SPU film before and after coating was carried out using XPS measurements. The N/C and O/C elemental ratios, calculated from the respective peak area of the C_{1s}, N_{1s}

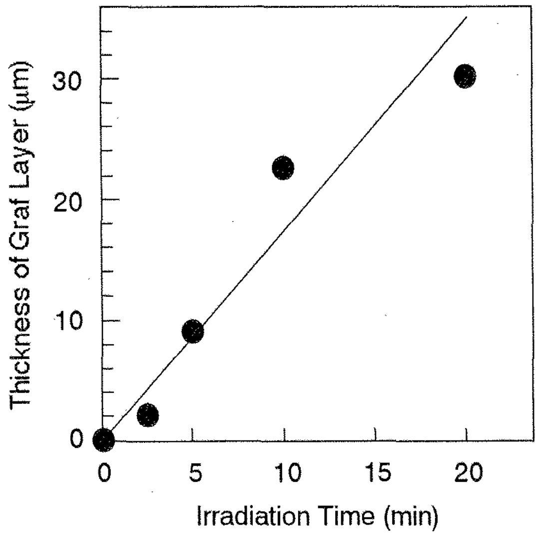

Fig. 4. Relationship between irradiation time and the thickness of the produced polymer layer on SPU film.

and O_{1s} signals and wettability are summarized in Table 1. After coating, the N/C ratio and the O/C one decreased from 0.25 (SPU) to 0.15, and 0.037 (SPU) to 0.022, respectively. The N/C and O/C elemental ratios of coated SPU films and their wettability data before and after irradiation are also summarized in Table 1. There was little difference in the elemental ratios before and after photoirradiation for nontreated SPU film. On the other hand, photoirradiation of camphorquinone-impregnated surface resulted in significant XPS spectral changes. The both elemental ratios upon photoirradiation increased from 0.15 to 0.18 (N/C), and from 0.022 to 0.13 (O/C), respectively. These values were close to the respective theoretical values for polyDMAAm (N/C = 0.2, O/C = 0.2). Little appreciable spectral change was observed after extensive washing with water. The irradiated, camphorquinone-impregnated SPU film surface exhibited a hydrogel-like characteristics upon immersion into water, and the surface become very wettable; the receding water contact angle was approximately 50° for the nontreated SPU surface and less than 5° for the irradiated, camphorquinone-impregnated surface (Table 1). Vigorous washing with water removed non-bound polyDMAAm but no delamination occurred. This surface modification proceeds with complex chemical reactions such as camphorquinone-initiated radical generation, polymerization, radical transfer, and radical recombination, thus resulting in surface graft polymerization and crosslinking.

When immersed into a rose bengal-containing aqueous solution, only the photoirradiated region and layer was stained. Since rose bengal is a fluorescence dye, the thickness of the graft layer was measured by confocal laser fluorescence microscopic observation. The thickness of the produced polymer layer increased with an increase of irradiation time (Fig. 4). A few tenths of hydrogel-like layer was obtained at longer irradiation time.

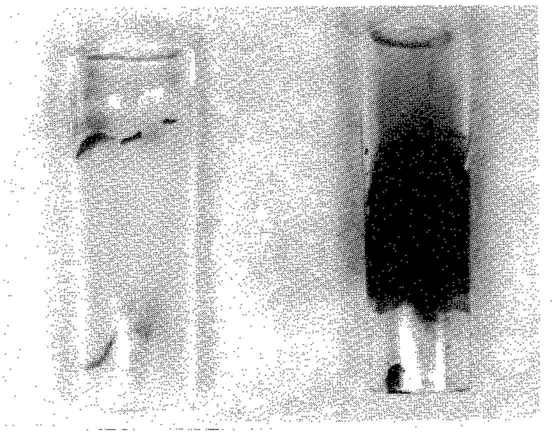

Fig. 5. Photograph of PVC tubes after contact with canine whole blood for 20 min. Nontreated PVC tube (right) and surface polymerized tube (left).

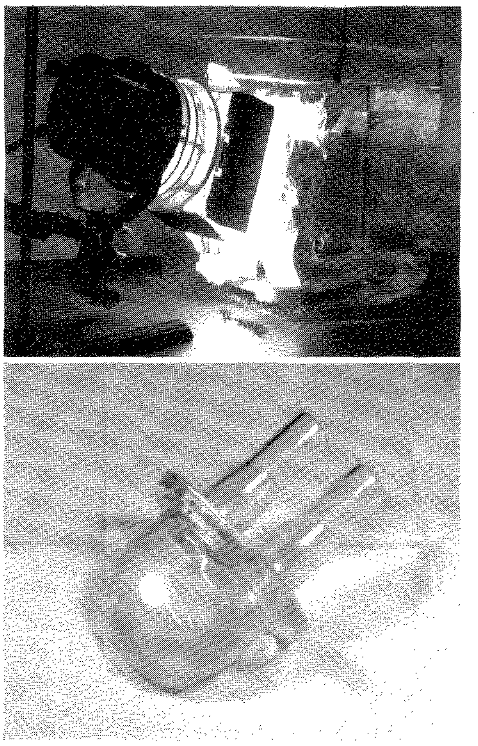

Fig. 6. Overview of the apparatus for the photopolymerization of the inner surface of the sac-type blood pump (upper) and the treated pump (lower).

3.2 Biological Response

The inner surface of PVC tube was graft photopolymerized with DMAAm, and then was contacted with canine whole blood for 20 min. In nontreated PVC tube, complete thrombosis formation occurred (Fig. 5). On the other hand, thrombus was significantly reduced on the graft-polymerized surface.

Especially thrombus formation was easily detached and removed upon gentle washing.

3.3 Application for Fabricated Device

The surface graft polymerization method was applied to a sac-typed blood pump (Univ. of Tokyo-type)[9,10] made of PVC. First, the inner surface of the pump was coated with camphorquinone-derivatized dodecane by immersion in a methanol solution. After air-dried, the blood chamber of the pump was filled with an degassed-aqueous DMAAm solution. Subsequently, the pump was placed into a water bath, and then photoirradiated with halogen lamp (800 mW/cm^2) (Fig. 6 upper). Upon photoirradiation (Fig. 6 lower), the inner surface of the pump become very wettable with water. Such surface-grafted pumps will be implanted to a goat to study whether or not blood-compatibility is upgraded. The result will be reported in the very near future.

4. Conclusion

The visible light-induced surface graft polymerization method was developed by surface impregnation of visible light-sensitive comphorqiunone derivatization. DMAAm-grafted surface was realized by visible light irradiation. This method may provide to confer potent biocompatibility to complex-shaped fabricated artificial organs.

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