Photo-Cross-linking of Polyvinyl Alcohol Containing Uracil in Concentrated Solution

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1. Introduction

Photodimerizations of pyrimidines (uracil and thymine) are known to occur by UV light irradiation (Fig. 1). Irradiation at 280 nm makes uracil into photodimer.1-4) Contrary to thymine, uracil does not have reversibility. However, sensitivity of uracil to photodimerization is higher than that of thymine.

The study of PVA containing uracil revealed that the PVA become insoluble by formation of one photodimer per one polymer chain.3,5) It was concluded that the effective photo-cross-linking was caused by hydrogen bonds between PVA polymers (Fig. 2).

This paper deals with the photo-cross-linking of PVA containing uracil units in concentrated aqueous solution, and with application of this system to medical use; embolization of cerebral aneurysms.

Microscopic neurosurgical treatments for cerebral aneurysms have become well established. However, there remain some cases with surgically inaccessible and inoperable aneurysms due to their size and/or anatomical situation. There are many successful reports on embolization of surgically difficult giant aneurysms. Detachable balloons and microcoils are used. However, the neck of such aneurysms is so irregular that complete occlusion of the neck by detachable balloon or multiple microcoils is sometimes impossible. A liquid embolus has a very flexible shape. If distal emboli from a liquid embolus could be minimized during embolization of aneurysms, it would be an ideal embolic material.

Two kinds of polymers were prepared as shown in Fig. 3. In PVA-1-Ura-e-2, uracil is linked to PVA by ester bond, and in PVA-1-Ura-e-8, uracil is linked to PVA with long alkyl spacer.

Fig. 1. Photodimerization of pyrimidines. 
R=H: uracil, R=CH3: thymine

Fig. 2. Photo cross-linking of PVA containing uracil.

Fig. 3. Uracil derivatives of PVA prepared.
2. Experimental

2.1. Materials

PVA-1-Ura-e-2 (1): PVA-1-Ura-e-2 (1) was prepared using the similar method used for preparation of uracil derivative of PVA in literature.

PVA-1-Ura-e-8 (2): The ester derivative of PVA having uracil having long spacer (2) was prepared according to Scheme 1. The imidazole derivative of uracil was obtained from 1-carboxyethyluracil with 1, 1'-carbonyldiimidazole (CDI). The obtained activated imidazole derivative (3) was added to the solution of ethyl 6-amino-n-capronic acetate (5) to give the amido derivative (6). After hydrolysis of the ester, the acid derivative (7) was activated again to the imidazole derivative with CDI. The solution of the activated uracil derivative was added to the solution of PVA (4) (PVA-217, KURARAY CO., LTD.) in dimethyl sulfoxide (DMSO). After dissolving of the imidazole derivative, catalytic amounts of sodium imidazole was added to the solution, and stirred for overnight at 50°C. The reaction was followed by TLC. The reaction mixture was poured into excess methanol-acetone (1:1) to give the polymer 2 as precipitates. Content of thymine units in PVA was determined by NMR spectra.

2.2. Photo-cross-linking of PVA derivatives

Photo-cross-linking was carried out in film and in concentrated solution. Films were prepared from aqueous solution of PVA derivatives on a quartz plate. The film was fully dried under reduced pressure. Irradiation of UV light was carried out at 265 nm and using a spectro-irradiator (CRM-FA, JASCO). The measurement of UV absorbance was carried out with UV/VIS spectrophotometer (Ubest-30, JASCO).

![Scheme 1. Preparation of PVA-1-Ura-e-8 (2).](image)

Fig. 4. Photodimerization of PVA-1-Ura-e-2 (□) and PVA-1-Ura-e-8 ( ) in aqueous solution. Uracil contents: 3.5-3.3 unit mol %, DP=1700, UV at 265 nm.

3. Results and Discussion

The absorbance of 265 nm peak derived from the uracil unit reduced according to progress of photodimerization with irradiation at 265 nm. This spectral change suggested photo-dimerizations of the uracil units in the polymer. Progress of photodimerization was followed by UV absorbance at 265 nm (Fig. 4), where UV absorbance was normalized. The rate of the photodimerization for the polymer with the long spacer units was higher than the polymer without the long spacer.

The films irradiated with 265 nm UV were developed in water to determine the reduction of solubility. The film not irradiated dissolved in water very fast. Therefore, the UV absorbance of the film represents the portion of cross-linked polymer.

In the case of photodimerization in solution, viscosity of the solution increased by photo-cross-linking. Solubility of the polymer in water decreased with photodimerization of uracil in PVA.

4. References